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THE TREATMENT OF ASTHMA

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BY

A. H. DOUTHWAITE

M.D., F.R.C.P. (LOND.)

ASSISTANT PHYSICIAN, GUY'S HOSPITAL
PHYSICIAN IN CHARGE OF MASSAGE DEPARTMENT, GUY'S HOSPITAL
HON. PHYSICIAN, ALL SAINTS' HOSPITAL

"To believe one knows is ignorance."
(HIPPOCRATES)

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PREFACE

THE admirable activities of the Asthma Research Council, in its efforts to elucidate the as yet baffling problems presented by bronchial asthma, have created a fresh and widespread interest in the disease.

The object of this book is to present an epitome of modern medical knowledge, particularly where this has direct bearing on the subject of therapeutics.

No claim whatever is made to originality, and the many English and foreign sources of information which have been drawn upon are freely acknowledged throughout the work.

The first part of the book is devoted to a consideration of asthma as viewed by the clinician and laboratory worker, for a clear conception of these two aspects is an essential preliminary to successful treatment.

The major section, dealing with therapeutics, has been written as far as possible without bias or dogmatism. Apart from many already widely accepted remedies, the author has

laid stress on the value of physiotherapy, and has described this subject, and that of vaccine administration, in some detail, prompted by considerable personal experience of these measures.

It is hoped that this book presents in an assimilable form all facts and theories of practical importance which are relevant to the subject, in order that those who lend their aid to the campaign against asthma shall be enabled to bring their knowledge up-to-date without the necessity of a laborious search through the vast literature which now exists.

That the majority of asthmatics can be materially helped by our efforts is certain. That only a minority can be cured is regrettable.

A reversal of this position can only be achieved by the closest co-operation between physician, specialist and biochemist, whose united efforts must inevitably lead to success.

A. H. D.

October 1930.

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THE TREATMENT OF ASTHMA

CHAPTER I

CLINICAL FEATURES

Definition.—The term "asthma" denotes a paroxysmal dyspnœa due to disturbed innervation of the bronchi, giving rise to their spasmodic contraction.

Clinical Aspects.—The practice of classifying asthmatics according to the apparent ætiology or exciting factors is confusing, and really does little to clarify the situation. Two main divisions stand out, however, clearly; namely, that in which patients have suffered from asthma since childhood (for convenience referred to as "primary asthma"), and that in which the disease has arisen at puberty or middle age, and has followed upon some respiratory disorder, e.g. whooping-cough or influenza (secondary asthma).

The former type not uncommonly gives a

history of eczema, urticaria or cyclical vomiting in childhood, and forms the majority of those patients in whom positive skin reactions to various allergens can be obtained in later life.

The second, or respiratory, type seldom evinces abnormalities other than the asthmatic paroxysm and possibly organic disease of the respiratory tract.

This clinical distinction has recently been upheld by Oriel (*q.v.*) (1), who finds marked differences in the biochemical features of the two groups.

Description of the Asthmatic Attack.— In an appreciable number of patients prodromal symptoms, which are constant for the individual, appear several hours before the actual paroxysm is initiated. These may consist of polyuria, the urine being of low specific gravity and colourless, intense lassitude, loss of appetite, flatulence, or mental depression. The attack usually comes on in the early hours of the morning, the patient then waking to find himself in the grip of the malady. If he be awake before the onset it is not unusual for difficulty in nasal breathing, profuse rhinorrhœa, sneezing, a sense of thoracic oppression, and itching of the skin

of the chest, back or neck to usher in the seizure.

It is a matter of minutes before the most urgent dyspnœa is established, in which the breathing though laboured is seldom appreciably increased in rate. The expiratory and inspiratory phases are both impeded in asthma, but owing to the relatively weaker power of expiration in the normal individual, this act is excessively prolonged when opposed by bronchial spasm. High-pitched wheezing during expiration is usually audible for many yards from the patient, who appears to be squeezing air out of his distended chest with every force at his command. As if to accentuate the effort a final expulsive jerk is performed before the commencement of the ineffectual heave of inspiration. The obstruction to the passage of air into the lungs is very evident on watching the contours of the thorax, for the supra-clavicular regions, the epigastrium, and the lower inter-costal spaces are sucked in during the effort.

If the hands be placed on the sides of the chest it will be observed that the actual expansion is very slight, the thorax being lifted as a whole, even at the end of expiration

presenting the position of inspiration of the chest in the healthy subject. The expanded state is due to the ever-increasing distension of the alveoli by the entrapped air, whilst the raised shoulder girdles are indicative of the forcible contraction of the accessory muscles of respiration, e.g. sternomastoid and part of the trapezius. The patient instinctively attempts to fix the shoulders in order to enhance the action of muscles passing from the thorax to scapula and humerus, and gains this object by grasping any stable article of furniture.

The change in facial expression is noteworthy. At first it is that of anxiety, the eyes widely open and staring, the forehead wrinkled. In a few minutes the colour pales and the lips part until the mouth is gaping, each inspiratory effort giving a downward twitch to the jaw.

An attempt at speaking seldom raises the voice above a whisper, because the force and volume of expired air is too feeble to allow of true phonation. The experienced asthmatic, however, never fritters away energy, but reserves his entire powers for the single purpose of breathing.

In many cases the attack passes off in an hour or two, sometimes rapidly, usually gradually. The subsidence is heralded by a cough, at first ineffectual, but later resulting in the expulsion of viscid sputum often in the form of pellets. A cold sweat starting on the face breaks out over the entire body, and occasionally the attack is closely followed by an extensive urticarial rash. The exhausted sufferer soon falls into a deep sleep, from which he awakes refreshed and in excellent health, in the early years of the disease.

Other attacks are more prolonged, lasting even for several days, but in such cases the paroxysm is never maintained at its full height throughout. Rather is there a waxing and waning of the dyspnœa without complete abatement. It is here that one observes the gradual development of cyanosis, profuse lachrymation and even hepatic enlargement, until death seems imminent, when sudden relaxation of bronchial spasm restores the patient to normal as if by magic.

Physical Signs.—Apart from the surface changes which have been noted, the signs produced within the thorax are very striking. Owing to the acute distension of the lungs,

the percussion note is generally raised in pitch and the heart dullness much reduced. Breath sounds are abolished and replaced by whistling and wheezing sounds, particularly noticeable during the long expiratory phase. Many years ago an observation was recorded by Salter (2) which can be readily confirmed, that these sibili, although audible at all points of the chest, appear and disappear at a given situation if this be under continuous observation. One gains the impression that although at any one moment the majority of bronchioles are in a state of contraction, yet at all times an appreciable number of these tubes are relaxed as if resting before springing into spasm again whilst their neighbours in turn seek brief respite.

Because of the lifting of the chest walls and depression of the diaphragm the heart's impulse can be felt in the epigastrium; the pulse is feeble, and at first but little altered in rate, but as the paroxysm advances the enfeeblement is accompanied by increasing rapidity, and falling blood-pressure.

The X-ray appearances of the lungs during an attack are similar to those of emphysema, namely, a high degree of illumination of the

pulmonary fields and flattening of the diaphragm. The latter feature accounts for the frequency with which the liver edge can be easily palpated, and it is probable that true enlargement of this organ from congestion is a rare event. In fact, the astonishing rapidity with which it recedes at the close of an attack is alone suggestive of replacement rather than of depletion.

The bronchoscopic findings in the larger bronchi are those of congestion, swelling of the mucous membrane and accumulation of mucus. Although, of course, direct observation of the finer tubes, which are the seat of spasm, cannot be made, nevertheless it seems reasonable to assume that in view of the continuity of the mucous membrane, the appearances are similar in the lower reaches of the respiratory tract. Following the injection of adrenalin, the membrane is seen to become paler and shrink.

The signs presented by the circulatory system during an attack are pallor of the skin, including that of the face, unless emphysema has already developed. In the latter event cyanosis will be observed from the commencement. If the paroxysm is prolonged, however,

cyanosis will develop in any case, and is most marked in the lips.

The blood-pressure almost invariably falls in spite of the muscular effort which is being made, and this is associated with a pulse of diminishing volume and force. The return of the pulse to its normal state at the close of a seizure is rapid and constant. Some authors have observed by means of X-rays the heart of asthmatic patients before and during an attack, and claim to detect a decrease in size in the paroxysm.

If the attack has been of considerable duration, râles at the lung bases, and widespread, high-pitched rhonchi may be detectable for several days, and are accompanied by variable amount of sputum which is occasionally blood-stained.

Sputum.—The most characteristic type of expectoration is composed of small, jelly-like pellets, semi-translucent and greyish-yellow in colour. They are embedded in tenacious mucus, but can be picked out when viewed against a dark background. When separated by shaking in normal saline, these bodies can be unravelled, and are found to be mucous casts of the finer bronchial tubes,

twisted in the form of spirals (Curschmann's Spirals). Epithelial, mononuclear and eosinophil cells are found in the sputum, the last type being characteristic, and occurring in greatest numbers in the spirals. Knott (3) has shown that the eosinophilia in the blood corresponds closely in degree to that of the sputum, a conclusion at variance with that of Alexander (4). In this connection it may be noted that the proportion of these cells in the blood may rise as high as 25 per cent. or more of the total leucocyte count.

Colourless octahedra, known as "Charcot-Leyden crystals," may be seen in the sputum, often within the spirals. The fact that they are found most easily in sputum which has stood for some time suggests that they are not actually formed within the body. Their chemical constitution is still a matter of doubt, and they are certainly not specific for this disease.

Immediate Cause of Asthmatic Paroxysm.—It is generally agreed that the respiratory distress of the asthmatic seizure is due to constriction of the bronchioles, brought about by spasm of the circular muscle fibres in their walls. The effect can be produced by stimu-

lation of the distal cut end of the vagus, and abolished by stimulation of the sympathetic fibres, e.g. by an injection of adrenalin.

The exact part played by mucous secretion and vascular turgescence has not been fully determined, but it is probably a minor one. Bronchoscopic findings suggest that vagal activity is associated with increased secretion of the mucous glands, and it is certainly the case that sputum is greatest in amount when the paroxysm is longest. In any case, however, it is inconceivable that the secretion can play an important part in the production of the dyspnœa which appears and recedes with such extraordinary rapidity.

Dilatation of the bronchial vessels no doubt accompanies an attack as a necessary corollary of increased muscular work, but there is no evidence to support the view that turgescence of the capillaries of the mucosa causes swelling of this membrane and consequent dyspnœa. In the first place, the mucous membrane of the bronchi is thin and not highly vascular in the human being. Secondly, asthma is not produced by the experimental obstruction of the pulmonary vein, in spite of the turgescence to which this step gives rise. Comparison

between man and guinea-pig in this connection is valueless because the bronchial mucous membrane in the latter is quite peculiar in its extreme vascularity.

General Characteristics of Asthma.—Certain features are presented by asthmatics with sufficient frequency to make them worthy of note, though it must be emphasized that many of them may be absent in individual cases.

Thus a family history of asthma, or migraine, or "nervous breakdown," or skin rashes following the ingestion of foods, such as strawberries or shell-fish, or contact with fur or certain flowers occurs with great frequency. Of these abnormal antecedents, the author has been most impressed by the frequency of occurrence in one or both parents of a vague malady referred to as "nerves," a point of interest in view of the theory of nervous instability embodied in Hurst's views of ætiology.

The paroxysmal nature of the attacks is a constant characteristic, and has been sufficiently described above.

Periodicity of seizures is often well marked in the earlier years of the disease. Thus some subjects suffer habitually in the early hours

of the morning: others are attacked weekly; others monthly; whilst a certain group are affected almost exclusively in one season of the year. The significance of these facts will be referred to later. It must be remembered that if the disease be unchecked, the attacks tend to greater frequency and individual length.

Retention of type in the individual is similar to that found in epilepsy. Thus the prodromal symptoms, the emotional reaction during the seizure, and the post-paroxysmal sensations are in many respects peculiar to each patient, and change but slowly with developing organic disease.

Change of type, though an apparent contradiction to the preceding remarks, is equally constant, but shows itself over intervals of many years only. The paroxysms become less clearly defined, last longer, but are usually less violent. The patient recovers more slowly, in fact some degree of dyspnœa persists throughout the day, and is accompanied by cough and expectoration. Change of type is in reality but an expression of change of structure and function of the respiratory and circulatory systems.

Sometimes the change may be more sudden and then not infrequently related to the appearance of another expression of allergy. Thus the author recalls a patient who, having suffered from asthma for many years, developed a sensitiveness towards chrysanthemums with which contact would produce a highly irritating papular erythema with underlying localized œdema. When this reaction occurred, she was free from asthma, and after five winters of contact with chrysanthemums, asthma disappeared completely, and has not recurred in the subsequent decade. On the other hand, this patient's skin now reacts in a like manner to contact with primulæ, and after the ingestion of strawberries.

Increased excitability to certain drugs, particularly those which stimulate the autonomic nervous system, can be noted in many instances. Thus a dose of pilocarpine, which would have no obvious effect on the normal individual, may produce profuse sweating and actually precipitate an attack of asthma if administered to the predisposed. In some cases heightened sensitiveness to adrenalin is likewise observed, suggesting a lack of stability on the part of the sympathetic

system. Genkin and Owtschinski (15) observe that some 50 per cent. of asthmatics give a vagotonic curve after injection of adrenalin, i.e. a fall of blood-pressure instead of a rise. Those who failed to show this nevertheless salivated excessively after pilocarpine administration. Again, they note that the blood sugar curve rises higher and subsides more slowly after adrenalin injection than is the case in normals.

Intercurrent maladies frequently abolish asthmatic attacks so long as the illness persists. Occasionally a cure is actually effected in this manner. If pulmonary tuberculosis supervenes in an asthmatic subject, the paroxysms become less frequent, less violent and soon cease altogether. Any acute febrile illness such as pneumonia or septicæmia has the like effect. As one result of fever is stimulation of the sympathetic it is probable that pyrexia acts in this manner to relieve asthma.

CHAPTER II

ORGANIC CHANGES RESULTING FROM ASTHMA

THE individual who has been the subject of asthma for some time usually presents deviations from the normal in physique and gait. Thus he is very thin, with rounded back and elevated shoulders which exaggerate the supraclavicular hollows. He walks with a stoop, and the trunk has but little movement, giving the impression of a clockwork figure propelled by action of the legs alone. The face wears a characteristically anxious expression, the skin of the forehead being thrown into transverse grooves, whilst the eyes are widely opened, slightly prominent, not infrequently bloodshot and watery. The mouth is often agape and the voice is hoarse, feeble and fluctuating in strength. A frequently repeated moist and ineffectual cough and slight duskiness of countenance are noticeable in long-standing cases.

Various deformities of the thorax may be

seen, especially in those cases in which asthma developed in childhood. The commonest is depression of the cartilaginous portions of the lower fixed ribs, but considerable indrawing of the corresponding part of the sternum is often a noteworthy feature. A most important change, from the point of view of treatment, occurs in the muscles of the thoracic wall and in some of those which pass from the chest to the spine or head, e.g. trapezius and sternomastoid. These structures tend to adopt a new postural length and tone, perpetuating as it were their abnormal state which is observed during an asthmatic attack. It is this fact which accounts very largely for the persistently raised shoulders, the inspiratory position of the thorax and the immobility of the trunk which have been noted to persist in the inter-paroxysmal intervals.

It will be clear that permanent incompleteness of expiration must lead to perpetuation of over-distension of the pulmonary alveoli, and it is probable that this state, bridging the gaps between the acute distension of the paroxysms, plays an important part in the production of true emphysema. The importance of correcting the muscular factor as a

first step towards successful treatment will at once be realized. In the confirmed asthmatic the increased muscular tonus seems, as it were, to overflow to all muscle groups, and gives to the patient a characteristic lack of suppleness and inability to relax.

The rounding of the back, at first produced in a temporary effort to increase the capacity of the thorax, ultimately takes on the character of a permanent deformity, again as the result of the spinal muscles failing to reassume their healthy state when the attack has passed off. In time the bodies of the vertebræ become reduced in the vertical depth of their anterior portions and take on a wedge-like form.

The lungs, at first the subject of intermittent over-distension (often unsuitably referred to as acute emphysema), fail after a few years to reach the normal position of expiration in the inter-paroxysmal intervals. This state of chronic distension produces the clinical signs of emphysema. In fact, the degree of true emphysema found after death in asthmatics is usually surprisingly less than that anticipated from bedside evidence. The importance of this observation is that so long

as textural atrophy has not occurred, much can be done to restore the lungs to their normal condition, whereas true emphysema is incapable of cure.

The effect produced on the bronchial tubes by repeated spasm of their muscle is difficult to assess because the majority of asthmatics develop chronic bronchitis and pulmonary changes due to circulatory weakness long before death. As, however, this knowledge is of no importance as regards treatment, the scanty observations on the subject will not be recorded; suffice it to note that an abnormal increase of thickness of bronchial muscle is found in the tubes of about 5 mm. diameter. Distal to this point the bronchioles have been found to be considerably widened, whilst on the tracheal side the muscular component rapidly regains its normal relationship to the other structures comprising the wall. If the increase of muscle bulk can be taken as an expression of augmented work, it is reasonable to assume that it is the bronchi of 4–6 mm. calibre which are involved in asthmatic spasm.

Demonstrable organic changes in the cardio-vascular system are rare even after many years of repeated attacks. During a paroxysm,

the output of the left ventricle is diminished, as evidenced by the small pulse, fall of blood-pressure and pallor of skin. At the same time the peripheral venous pressure rises to two or three times the normal height, for the return of blood to the right side of the heart is seriously impeded. This obstruction to flow is occasioned by the diminution of the difference between intra-thoracic and atmospheric pressures. The lungs, being inflated to an extreme degree by entrapped air, lose the effectiveness of their normal tendency to recoil, whilst the powerful expiratory efforts not only abolish the negative intra-thoracic pressure, but convert this into a highly positive factor. An important aid to the return of blood is thus lost and venous congestion becomes a prominent feature.

Again, the passage of blood through the pulmonary vascular bed is impeded particularly during the violent efforts to expel air, and this state of affairs coupled with imperfect alveolar ventilation occasions a fall of oxygen saturation of the blood.

The signs suggestive of cardiac failure which may be seen in prolonged attacks are in reality due to the obstruction of venous return

together with reduced oxygenation. There is no evidence to support the view that the right side of the heart is distended with blood on account of pulmonary obstruction. It seems rather as if it were starved of blood because of the disturbance of the normal relationship of intra- and extra-thoracic pressures.

It appears that the various units of the circulatory system can withstand the repeated insults of the asthmatic paroxysm and show no change for the worse for many years. In fact, it is doubtful whether the heart is ever permanently affected by asthma directly, although indirectly this does arise by virtue of the production of emphysema.

With development of the latter condition, the ensuing textural destruction of the lungs brings with it a diminution in the size of the pulmonary capillary bed, and thus imposes a direct tax on the powers of the right ventricle. In addition to this, the resulting loss of elasticity of the lungs incurs a corresponding loss of one of the most important aids to the completion of the circulatory circuit, thereby producing a state of chronic venous congestion which is so apparent in the emphysematous subject.

It follows from this that the coronary circulation must suffer in like manner.

We find very good reasons, therefore, for hypertrophy of the right ventricle to develop, and for the heart muscle as a whole to undergo fibrotic changes which ultimately lead to its failure. By the time that death occurs, myocardial disease is usually so extensive that a marked disproportion between the right and left sides of the heart is seldom found, although often confidently postulated by the physician.

The occurrence of hepatic engorgement, albuminuria and œdema may, of course, be regarded as a final result of lifelong asthma, the immediate cause being circulatory failure engendered in the manner described.

CHAPTER III

DIFFERENTIAL DIAGNOSIS

Bronchial asthma such as we have discussed occurs in its pure form as a periodic symptom complex unassociated with any other disease. Precisely similar paroxysms develop not infrequently, however, in middle-aged persons, the sufferers from chronic bronchitis. To this condition the term "bronchitic asthma" or "asthmatic bronchitis" might be applied, although it is probable that ætiologically it differs but little, if at all, from our second, or respiratory, type of bronchial asthma referred to in the first chapter. Clinically there is this difference, that whereas the latter appears to deviate in no way from the allergic type of asthma, so far as the physical signs are concerned, but is recognized by the immediate precursor of the first attack being some respiratory disease, yet bronchitic asthma is fundamentally associated with bronchitis throughout its existence. It arises after a more or less lengthy period of bronchitic

attacks, is ushered in by an outbreak of bronchitis, and for many weeks after the paroxysm signs of bronchitis persist. By the nature of things, it would be expected that bronchitic asthma would occur in the colder months of the year, and this is, in fact, the case. Cough is, of course, an outstanding symptom here and precedes the onset of asthma by several days or weeks and follows it for a like period. On the other hand, primary or allergic asthma is, as we have seen, closed by a bout of coughing but not heralded by it.

At the risk of tiresome reiteration it is again emphasized that many of these distinctions are important from the clinical and therapeutic standpoint, but probably depend for their origin on closely allied ætiological factors. Nevertheless, as will be shown later, a definite biochemical difference exists between the primary and secondary types (Oriel), yet if bronchitic asthma is but a variety of the latter its recognition is not pointless when the all-important question of treatment is under consideration.

Cardiac Asthma.—Attacks of asthma which occur with, and are due to, severe disease of

the heart undoubtedly occur, though infrequently. Cardiac asthma is a totally different thing from cardiac dyspnœa, in fact, it simulates bronchial asthma very closely. The attacks usually occur at night, in the early hours of the morning; they are paroxysmal in nature, and, so far as the type of dyspnœa and lung signs are concerned, indistinguishable from the disease with which we have dealt.

The diagnosis is, however, seldom a matter of difficulty, because a history of long-standing dyspnœa on exertion, swelling of ankles, recognition of the existence of high blood-pressure, or disease of the heart, is almost certainly to be elicited. Furthermore, examination reveals obvious disease of the heart in a patient long past the usual age for bronchial asthma to arise.

The cases of cardiac asthma seen by the author have usually been those in which hyperpiesis and extensive arteriosclerosis have been present, often in association with coronary thrombosis.

The development of this symptom is of serious import, and not uncommonly merges into acute œdema of the lungs.

The actual mechanism of its production is

a matter of doubt, but is probably related to the condition of chronic congestion of the pulmonary vascular system.

In passing, it may be mentioned that, in spite of theoretical objections to the contrary, the administration of morphine is the best treatment to relieve the immediate distress.

Renal Asthma.—Again, a typical asthmatic attack is seen, but a general examination of the patient will at once reveal the raised blood-pressure, dry tongue, hypertrophied heart, arteriosclerosis and albuminuria indicative of chronic interstitial nephritis. Renal asthma is rare, and occurs almost only when clear evidence of uræmia is forthcoming. An examination of the retinæ seldom fails to indicate the nature of the disease with which we are faced.

The prognosis and treatment are those of uræmia.

Pulmonary New Growths.—A somewhat rare symptom of a neoplasm of the lung is a typical asthmatic attack. The possibility of underlying disease of serious nature should be suspected when asthma arises in patients in the fifth decade or later.

An example of this condition was presented

by a lady of sixty-five years who was seized by urgent dyspnœa in the early hours of the morning. The physical signs were indistinguishable from those of bronchial asthma, and the spasm yielded to injection of adrenalin. In the interparoxysmal intervals no abnormality could be detected for several weeks. Eventually restriction of movement of the right side of the chest was noticed, and ultimately the patient died of an infiltrating carcinoma of the bronchus.

Similar cases have been recorded by other workers.

Certain Types of Dyspnœa.—To this point we have considered the differential diagnosis of certain morbid states in which true asthmatic paroxysms occur. It may not be out of place to examine types of dyspnœa which are from time to time confused with that of asthma, although due care should prevent the committal of such errors.

In the first place, cardiac dyspnœa is characterized by its intimate association with muscular effort, the one increasing commensurately with the other. It is usually aggravated by recumbency. In type, it is panting, gasping and accelerated, but there is none of

the prolonged forced respiratory phases presented by the asthmatic. A considerable degree of cyanosis and other signs of circulatory embarrassment are seldom wanting.

The dyspnœa of bronchitis has a greater similarity to that of asthma than has that of the preceding type. In fact, some degree of bronchial spasm undoubtedly occurs from time to time in the course of the disease. The frequent interruption of breathing by cough, the expectoration of considerable sputum, the basal râles, and the absence of the fight for breath one observes in asthma should help to settle the diagnosis.

It has, of course, been pointed out that bronchitic and emphysematous dyspnœa can become grafted on to that of asthma, but in such patients the history will point to the sequence of events.

CHAPTER IV

STUDIES IN METABOLISM AND BACTERIOLOGY

The recent and as yet uncompleted research of Oriel (1) into the biochemistry of asthma has revealed the presence of certain deviations from the normal which are likely profoundly to influence the course of treatment adopted.

For many years past Osman (5) has directed attention to the low sugar reserve in certain children exhibiting diseases of the allergic group, including asthma. Oriel, working in this connection, has demonstrated the presence of a low blood sugar in both the primary and secondary forms. Thus if the normal blood sugar content expressed in milligrammes per 100 c.c. be taken as 85 to 100 whilst fasting, and the figure half an hour after taking 50 grammes of glucose as 120 to 150, in the asthmatic the corresponding figures are 74 and 117, with return to the original level in two hours or considerably less.

Another observation of great interest is the presence of a positive Van den Bergh reaction in the majority of asthmatics of the first or primary type only. The reaction is positive during the asthmatic attack and is a delayed biphasic direct and a delayed indirect. For those readers who are unfamiliar with the details and significance of this test it may be stated that it consists of the addition of Erlich's diazo reagent to the patient's serum. A positive result is shown by the appearance of a red or purple colour and indicates the presence of bilirubin. Depending upon the colour produced and rapidity of its development are based the conclusions as to the exact nature of hepatic derangement. In the instance quoted, the reactions point to liver damage such as occurs in toxic and infective jaundice.

Barber and Oriel (24) summarize the biochemical changes which take place in allergic states, including asthma, as follows: Immediately preceding and during the attack the amino-acid and uric acid content of the blood rises: the chlorides fall. The urinary free acidity rises; the urine is concentrated and deposits urates on cooling: chlorides are diminished: the ether reaction (Chap. VIII)

is strongly positive. Ammonia, amino-acid, creatinine and uric acid excretion rises.

Following the paroxysm the changes in the blood are reversed, as are also in the main those of the urine.

Note that the injection of foreign proteins in animals produces an increase of the blood amino-acids and eosinophilia.

Bellingheimer (11), Franke (12) and others (15) note a reduction of blood calcium in the asthmatic. There may be an abnormally low total calcium, or more commonly the proportion between active (ionized) and combined calcium is disturbed to the disadvantage of the former. In view of the fact that calcium ions depress vagus conductivity it will be appreciated that a reduction in their concentration will lend itself to the occurrence of asthma.

The above results indicate that at the time of an asthmatic paroxysm, there exists some degree of hepatic derangement and acidosis. Towards the end of an attack there is a swing over to alkalosis, a fact which may account for the diuresis which not uncommonly follows a seizure.

Various urinary abnormalities are also to be found, the one having the most direct

bearing on treatment being the presence of a proteose, probably the cause of the ether reaction, which is excreted during an attack in the allergic type of asthmatic and in many other allergic diseases. When isolated and injected intradermally in minute doses even as low as one part in a million it produces a positive reaction in the nature of a wheal. Larger quantities may precipitate an attack of asthma. It has no effect on normal individuals, neither is an active substance of this nature to be found in their urine. Furthermore, it tends to disappear from the asthmatics' urine between the attacks. Oriel's proteose seems to be specific in so far that it produces skin reactions only in asthmatic subjects and not in those of other allergic diseases. On the other hand, he has isolated a proteose from the urine of several of the author's cases of rheumatoid arthritis and the substance has produced the same type of skin reaction as in asthma, and an overdose has caused an acute exacerbation of joint symptoms. Here again, however, evidence of hepatic insufficiency was forthcoming. The fæcal bacteriology in both diseases presenting these abnormalities has been very similar.

It is possible that the proteose represents a fraction of a protein which has been partially broken down in the gut and then absorbed. The deranged liver fails to complete the destruction of this body, which circulates in the blood as a potent excitor before being excreted by the kidneys.

That an antigen can pass from the gut into the blood-stream is indicated by the Prausnitz-Küstner reaction. This consists of injecting serum from a person known to be sensitive to a certain protein, e.g. egg, into the skin of a normal individual. If the latter now eats an egg, a wheal is produced at the site of the injection.

In a recent article by Oriel and Barber (26) further observations are recorded of the behaviour and possible origin of this complex substance which for convenience is designated simply as proteose. Serum from a subject actually suffering from migraine (believed to be another allergic disease) was injected intradermally at two points into the arm of one of the authors. A small quantity of a 1 in 10,000 solution of the proteose from the same patient was scratched into one of these sensitized areas on the following day. A

brisk reaction in the form of a wheal developed. No reaction was produced by the introduction of the proteose into unsensitized skin, neither did it appear when the second sensitized spot was treated with proteose from an asthmatic patient.

The extraordinary specificity of this substance is thus demonstrated and the conclusion is reached that the proteose contains the active antigen.

The subject will be pursued farther when dealing with the preliminary investigations of a case of asthma.

Studying the flora of the fæces, Knott (3) has found that a considerable number of asthmatics showing signs of hepatic derangement as described above have foul, alkaline, proteolytic stools containing excess of imperfectly digested muscle fibre and giving rise to abundant growth of bacilli of proteolytic type. Taking this fact in conjunction with the finding of Oriel's proteose, a close connection between protein decomposition in the gut, liver derangement, the circulation of abnormal protein products and the occurrence of asthma is strongly indicated.

On the other hand, in the larger group of

asthmatics exhibiting no other allergic manifestations, and in whom the original paroxysm was related to a respiratory disease, none of the above-named peculiarities is to be found. By analogy it seems probable that their attacks are activated by some other foreign protein possibly derived from bacteria.

Knott (22), in a recent communication concerning the fæces of 120 asthmatics, found excess of undigested protein in 37 ; excess of starch in 17 ; excess of starch and protein in 7 ; normal stools in 59. Late-lactose fermenting bacilli occurred with great frequency in the stools with excess of starch, and rather less so in those characterized by undigested protein. The proportion of the normal fæces containing these organisms was extremely small.

No definite conclusions have been reached in connection with the bacteria found in the sputa of asthmatics. Haibe (6) claims to have found a hæmolytic streptococcus in 80 per cent. of patients belonging to the second type. He states also that intradermal injection of the toxin gives a brisk reaction which cannot be reproduced after a course of vaccine treatment. The organism was isolated from the pellets.

Knott (3), on the other hand, also cultivating from the plugs and spirals, finds that "there is no one type of organism which occurs with special frequency in the sputum of asthmatic as compared with non-asthmatic patients, except possibly certain gram-negative bacilli." The latter are possibly identical with Bacillus Friedlander and influenzæ.

Finally we find that hypochlorhydria is a common feature of the asthmatic's gastric juice. It occurs with much greater frequency in the young allergic type, whereas in the secondary form its coincidence is probably no more than would be found in normal individuals. Bray (23), reporting on the result of a hundred fractional test meals in children aged six months to ten years, states that in 12 per cent. no free hydrochloric acid was found and in 45 per cent. never more than ten units. It has yet to be determined whether any connection exists between hypochlorhydria and the formation, circulation and excretion of proteose, and whether the deficiency of hydrochloric acid is secondary to a gastritis or of congenital origin.

CHAPTER V

ÆTIOLOGY

THERE can be little doubt that in asthma hyperexcitability of the parasympathetic system plays a dominant part in the production of the attacks. The susceptibility to pilocarpine already noted supports the view. Furthermore, in view of what has been written in regard to the mechanism of the disease, it seems clear that the vagal centre, or vagus, is unduly sensitive to stimuli and consequently gives rise to broncho-constriction. An inherently hypersensitive bronchial centre has been postulated by Hurst (7) whilst increased sensitivity of the vagus has been suggested by McDowall (8).

The fact that sympathetic stimulants, e.g. adrenalin, tend to abolish asthmatic attacks again points to the lack of balance between parasympathetic and sympathetic systems.

Although parasympathetic preponderance is no doubt an inborn and often inherited characteristic of the first type of asthmatic,

it seems equally certain that vagal hyper-excitability at any rate can be acquired in later life, as, for instance, in a large number of patients who develop the disease after influenza or bronchitis. In other words, an asthmatic diathesis does not exist in all instances. Oriel's researches have already gone a long way to show that the biochemical abnormalities are largely confined to one group.

Of recent years attention has been directed towards the phenomena of anaphylaxis and the similarity of this state with that of asthma. The idea arose from the observations of Meltzer on the condition of the lungs and bronchi in guinea-pigs dead from anaphylactic shock. It will be remembered that the production of anaphylaxis depends upon the reinjection of a foreign protein after a lapse of ten or more days. The resulting reaction depends to a certain extent upon the animal in use, but a rapid fall of blood-pressure, vomiting, collapse and bronchial spasm may occur. Guinea-pigs are prone to the latter, and it is well to recollect, when drawing comparisons with the human being, that their bronchial mucous membrane is peculiarly vascular.

True anaphylaxis occurs in man, though not

so readily as in animals, usually after the administration of foreign serum to a patient who has been sensitized to this substance at an earlier date. Pallor, sweating, eosinophilia, fall of blood-pressure and collapse occur, and in the event of recovery the alarming symptoms may be followed by widespread urticaria (*comp.* asthma). On the other hand, bronchial spasm is not noted.

It is clear, then, that an asthmatic attack is not a phenomenon of true anaphylaxis, although there are points in common between the two conditions.

That the asthmatic reacts abnormally to certain foreign substances will be evident when reviewing the exciting factors of the seizure, and this hypersensitivity is now referred to as "allergy." There are many allergic reactions, of which asthma is one, urticaria another, hay-fever another. Why it is that different symptoms should be produced in different patients, who nevertheless show the same biochemical deviations, is difficult to explain. Again, in the course of his life a patient may exhibit consecutively various manifestations of allergy, e.g. eczema in childhood and asthma in later life.

Barber and Oriel (24) emphasized the significant fact that the same essential cycle of biochemical events takes place in all the allergic conditions which they have investigated, in spite of the differences in the symptom complexes.

They state that the changes in blood and urine are such that from the results of their examination they can with some degree of confidence recognize the stage of the patient, pre-paroxysmal, paroxysmal and post-paroxysmal, at which the specimens were collected.

Freeman's (9) view that local tissue damage with histamine liberation is potent in focusing allergic manifestations at certain points is probably in the main correct. Thus in the predisposed individual repeated catarrhs, whooping-cough, influenza and other respiratory diseases are prone to be followed by asthma.

In infancy the skin and digestive tract are more exposed to trauma, whence the occurrence of infantile eczema and " bilious attacks " in children who in later life develop asthma. The distribution of the eruption in eczematous cases is then explained, for it is the flexures which are attacked, and these particularly at

the groins, which are subject to excessive heat and moisture.

Sutherland (21), in an admirable general survey of asthma, points out that the phenomena of pure asthma can all be produced by histamine. This substance, if injected into guinea-pigs in which the medulla has been destroyed, gives rise to intense bronchial spasm, which can be counteracted by adrenalin and prevented by atropine.

It is suggested that in hay-fever, for instance, pollen falls on the mucous membrane and, being absorbed, encounters the specific atopic reagin, with resulting liberation of intense poison. This in its turn damages the tissues, with consequent histamine production.

Allergy is further distinguished from anaphylaxis by the fact that the latter can be induced by almost any soluble protein and not by other organic substances. On the other hand, allergic reactions are well known to occur as the result of exposure to ipecacuanha, alcohol, acetylsalicylic acid and other non-protein compounds.

Again, allergism appears to be an inherited tendency, whereas anaphylaxis is essentially an acquired abnormality, the phenomena of

which, moreover, can seldom be reproduced when once an attack has been overcome.

The clinical conditions hay-fever, asthma, infantile eczema, urticaria, angio-neurotic œdema and cyclical vomiting are now accepted as manifestations of allergism. Two or more co-exist, or follow each other, or again alternate. One is evidently observing a tissue reaction in the nature of exudation or muscle spasm initiated by the arrival of the particular allergen, e.g. pollen, which evidently depends upon the presence of an unidentified substance in the serum for its effects. The latter statement is supported by the transference of localized allergism to the normal individual by means of serum (Prausnitz-Küstner reaction, *q.v.*); this substance is known as "atopic reagin."

Some suggestive experiments have been carried out by Oeller (16) and Schilling in injecting guinea-pigs with chicken erythrocytes which are nucleated and recognizable for several days. Reinjection results in hæmolysis of these cells, which in the lung is accompanied by capillary and lymphatic dilatation and accumulation of eosinophils. An exudate forms in the bronchioles very similar to that of asthma and containing many

eosinophils. These facts, taken in conjunction with the accepted observation that eosinophils also collect in the neighbourhood of the point of introduction of foreign protein, suggest that their function may be to destroy the injurious agent.

If we admit that bronchial asthma can be a manifestation of allergy, are we justified in concluding that this is always the case ?

Memory will at once serve us with cases from which asthma has been eradicated by the removal of a morbid source of reflex stimulation, e.g. nasal polypi, infected ethmoid and so on. It is perfectly clear that a focus of constant irritation can give rise to periodical muscle spasm, e.g. intermittent spasm of the orbicularis oculi in the presence of chronic conjunctivitis. It seems unnecessary, therefore, in many such instances to invoke the aid of allergy to explain asthma, particularly when nasal disease is present.

Experimentally the most certain way to produce broncho-spasm is to stimulate the posterior and upper part of the nasal septum. We see here a pure reflex effect which should have its parallel in human pathology.

Again, the development of asthmatic attacks

in cases of bronchial carcinoma must surely be of reflex origin.

It is true that many individuals have infected nasal sinuses, polypi, and so forth, yet never suffer from asthma. But this merely brings us back to Hurst's dictum that a hyperexcitable broncho-constrictor centre must be present. The hyperexcitability may be inborn, or acquired as the result of repeated stimulation of submaximal intensity, or as the result of the action of bacterial toxins.

In the first chapter it was pointed out that clinically a differentiation of bronchial asthmatics into two main types is readily discernible. Later it was shown that Oriel had established this division on the result of his biochemical studies.

As against this we have Knott's (3) statement that the frequency with which eosinophils are found in the mucous plugs and spirals is about the same in both types. He finds the same to apply to the eosinophilia in the blood, and concludes "... eosinophilia appears to indicate simply the presence of true asthma, ... but does not differentiate the type."

The significance of eosinophilia in relation to the question which we have posed is that it is

a constant finding in many forms of allergy, e.g. during an attack of hay-fever (4), and is furthermore produced experimentally by the injection of foreign protein into animals (8). A local accumulation of eosinophils also occurs at the site of injection of the protein, and is found in the sputum of asthmatics, nasal discharge in vaso-motor rhinitis and skin lesions in urticaria. That a close relationship exists, therefore, between eosinophilia and the presence of foreign protein or protein derivatives in the blood is demonstrated, and supports the view that the majority of cases of asthma are allergic in nature.

If this be so it is reasonable to conclude that in asthma following respiratory or sinus infection the body has become sensitized to bacterial protein. The removal of a localized nidus of sepsis would, therefore, result in disappearance of the asthmatic attacks on the same grounds that a sea voyage will bring relief to the subject of hay-fever. Similarly the undoubtedly beneficial action of vaccine therapy in certain forms of bronchitic asthma is explained.

On the other hand, McDowall (8) points out the significant fact that stimulation of the

vagus causes a fall of blood sugar owing to insulin liberation, which may be responsible for eosinophilia. As it is clear that vagal stimulation is a necessary precursor of the asthmatic attack, it seems possible that eosinophilia is not to be regarded as an indication of the presence of foreign protein in the circulation.

In any case we are left with a small number of cases presenting evident sources of reflex irritation in which no allergic signs, including eosinophilia, are forthcoming.

It would seem, then, that although the majority of asthmatic attacks provide evidence of allergism, a definite minority owe their symptoms to a simpler process of reflex irritation alone.

CHAPTER VI

PROVOCATIVES OF ASTHMATIC PAROXYSM

ASTHMA is but an expression of an underlying constitutional derangement and ultimately depends for its production on vagal stimulation. The factors which may disclose this tendency are as varied in character as they are numerous.

Allergens.—In the first place we have a vast array of substances which, if brought into appropriate contact with the human body, produce the allergic reactions we have considered. A large group consists of those normally encountered in the atmosphere which reach the blood-stream through the respiratory tract. Various grass pollens are well known to excite attacks of hay-fever, not infrequently accompanied by asthma. The dust of certain woods, e.g. rosewood and sandalwood, or of ipecacuanha, and a common ingredient of face powder, viz. orris root, may act as powerful provocatives

of spasm. Moulds in the dust of rooms may be most elusive excitants, difficult to identify and resistant to elimination. It is a well-recognized fact that asthmatics may suffer nightly torture in their own homes and yet be free when staying in other houses, and vice versa. In the one case this may be due to escape from the proximity of an allergen in the nature of pollen, in another a mattress in daily use may become impregnated with a particular mould, e.g. *Aspergillus fumigatus*, in which case a change of bedding will obviate the attacks for several months. Yet again, the patient may be sensitive to the feathers with which his pillows are stuffed, or the presence of some pet animal in the house may be inimical to his well-being.

Animal emanations often function as powerful allergens. Thus contact with horses, cats, or dogs and so on will produce paroxysms of asthma in the correspondingly susceptible individual. The mere presence of such an animal in the room may be sufficient to bring on an attack, and even contact with riding breeches which have been out of use for many years can precipitate a seizure in a "horse asthmatic." It is usually the epidermal cells

which cause the trouble, in fact, the patient often fails to react to contact with other parts of the animal's body.

Allergens gaining access viâ the alimentary tract are numerous. Food asthma is detected most commonly in patients who have developed the symptoms in childhood, and it is not surprising therefore to be able to incriminate cows' milk or eggs.

A high degree of specificity is demonstrable in relation to allergens. An individual may be prostrated by asthma as the result of eating a food in the preparation of which a hen's egg has been used, yet is able to enjoy free consumption of ducks' eggs. Again, he is seldom sensitive to chicken flesh or feathers, although this is not invariably the case.

Aspirin, ipecacuanha, alcohol, coffee, pyramidon and many other drugs produce allergic symptoms in the predisposed, the first named being the commonest, probably because of its widespread use.

It should be noted that asthma can be produced by the administration of the above-mentioned substances by different routes to those along which they usually approach the body. Thus the injection of Timothy grass

pollen will occasion intense rhinorrhœa, lachrymation and asthma in the hay-fever subject.

The possibility of bacterial allergy has been mentioned when considering those cases of asthma intimately related to focal infection. That it can exist seems probable on analogy with the instances we have just discussed, but whereas the provocative nature of horse dandruff, pollen, etc., can be shown by skin and other tests, this is by no means so clear in the matter of micro-organisms.

Local Irritants.—Direct irritation of the bronchi is a common source of asthmatic attacks. Thus it is probable that chronic bronchitis acts in this manner in many instances. Again, exposure to irritant gases employed in manufacturing processes, or in the course of war, may be the immediate cause of broncho-spasm. Asthmatic attacks once started thus may persist in spite of the patient having been removed from the noxious environment.

Reflex Stimulation.—The vagus may be stimulated directly or indirectly from various sources. Thus an overloaded colon or distended stomach commonly gives rise to asthmatic attacks. It is probable that asthma

precipitated by abnormal conditions of the alimentary tract, or by the ingestion of certain foodstuffs, is to be explained in some as direct reflex irritation, in others as the result of absorption of material which acts as an allergen. Thus flatulent distension of the stomach and constipation presumably function reflexly, for the paroxysm may be cut short by prompt measures to relieve the underlying condition.

The importance of the part played by gastro-intestinal disturbances in this connection cannot be over-rated. A vast number of asthmatics, including those for whom a specific allergen has been detected, are prone to repeated attacks if they eat liberally, and particularly if they take a meal of any size after the early hours of the afternoon.

Salter was the first to point out that reflex action could not account for all these cases of alimentary asthma. He observed that asthmatic attacks related to certain foods appeared after the interval of time which must elapse before they reached the blood-stream. Thus alcohol will in the alcohol-sensitive asthmatic precipitate an attack within a few minutes of ingestion, whilst egg or milk produces no ill-effects for a number of hours. This observa-

tion comes into line with the modern views anent allergy.

Pickering has shown that in certain conditions of the alimentary tract imperfectly digested protein may enter the blood, probably in the form of peptone, and initiate an attack. This fact explains in part the importance of a suitable dietary for asthmatics, and also the inadvisability of using purgatives. The latter are obnoxious because by their irritation they hasten the absorption of proteins which have been hurried in transit and imperfectly digested.

Indirect reflex stimulation of the vagal centre is well exemplified in patients in whom nasal disease is found and who recover completely when this is eradicated. The importance of the septum in the experimental production of broncho-spasm has been referred to already. In asthmatics of this type the usual findings are polypi, ethmoidal infection or an enlarged middle turbinal which is apt to make contact with a deflected septum.

The significance of the part played by nasal disease in the production of asthma has, however, been grossly exaggerated. A temporary improvement in the patient's condition follows some intra-nasal operations such as

cauterization of the septum with great frequency, sometimes because of destruction of nerve endings in a highly broncho-spasmogenic centre, sometimes because the flow of impulses arising as the result of operative trauma blocks the reflex path of the impulses arising from some totally different asthmogenic point.

In matters of ætiology there is the ever-present danger of putting the cart before the horse. It is well, then, to note that Rackemann and Tobey (19), and more recently Gill-Carey (20), consider that local lesions of the nose and throat may develop from the same fundamental cause as asthma. For instance, repeated rhinorrhœa, which may be a most distressing symptom of asthma, may give rise to an œdematous condition of the mucous membrane and polypoid growths.

Psychical Influences.—That the higher functions of the brain are capable of profoundly influencing the lower levels of the nervous system is a well-proven fact. In no diseases is this better illustrated than in asthma.

Mental associations are formed between certain objects or places and asthmatic attacks. Ultimately the reaction becomes that of a conditioned reflex. There are many examples

of patients, definitely sensitive to a particular object, e.g. a cat, being gripped by an asthmatic seizure in the belief that the dread excitant was in their close neighbourhood, only to find that they had been mistaken in their fear.

Again, most of us have met the type which develops attacks of asthma whenever there is a possibility of receiving a dose of morphine, which was originally introduced to him to cut short an obstinate broncho-spasm. Furthermore, such an attack may often be overcome by the hypodermic injection of water, yet of the truly asthmatic nature of the dyspnœa there can be no doubt.

Undue stress has undoubtedly been laid on the possibility of asthma being a psycho-neurotic manifestation. Moos (13) is greatly impressed by the efficacy of psycho-analysis in the treatment of this condition. The true position is presented by Gillespie (14), who finds that from the psychological point of view asthmatics fall into three classes. A small one in which the attack has the same status as a neurotic symptom. A second group in which asthma is independent of a co-existing neurosis, but in which emotional causes may precipitate an attack. A third group in which

nervous symptoms are definitely secondary to the disability of asthma.

Endocrine Excitants. — A common feature in women is the coincidence of asthmatic attacks with the onset of menstruation. Some patients suffer only at these times, but more often one finds that though not infrequently asthmatic in the intermenstrual intervals they can rely on prolonged and frequent outbreaks at the time of the periods.

It is possible, of course, that this is also another example of reflex disturbance, but in view of the relative frequency of the association of the menstrual cycle with asthma, as compared with that of other possible sources of reflex stimulation, one cannot but assume that the alteration in functional relationship between certain ductless glands which takes place at this time must be responsible for the production of the asthmatic symptoms. The precise nature of the changes is still a matter of conjecture, but it is no doubt associated with the partial antagonism which exists between the suprarenal medulla on the one hand and the adrenal cortex and ovary on the other. At the time of menstruation there is heightened activity of ovary and suprarenal cortex. The

latter is evidenced by an increase of blood cholesterol and choline (10). The latter substance is an antagonist of adrenalin and will therefore depress sympathetic activity and enhance that of the parasympathetic, including the vagus. The occurrence of broncho-spasm is thus explained. It is a matter of common observation that pregnancy, on the other hand, results in disappearance of asthma temporarily. The paroxysms usually return towards the end of the lactating period. Less often the exact opposite occurs, asthma revealing itself only during the period of gestation.

Some German authors consider the appearance of asthma in the male at the commencement of coition to point to a state of temporary endocrine imbalance as being the provocative factor. In these instances the connection between sexual act and asthmatic paroxysm is so close that an hormonic origin seems scarcely possible. Furthermore, so far as is known, the only ductless gland which immediately exhibits heightened activity is the suprarenal medulla. The explanation must lie in the psychic or reflex causation.

Miscellaneous Provocatives.—A sudden cough or laugh may be responsible for the immediate

onset of an asthmatic attack. Probably these cases are but examples of reflex stimulation of the bronchial centre. A realization of the danger of mirth is soon developed in the asthmatic, and it is a rarity for a patient to give vent to a hearty laugh, even though he be in no way depressed in spirit by the knowledge of his disability.

Violent exercise is also prone to initiate a paroxysm because of the disturbance of acid-base equilibrium towards acidosis which occurs in these circumstances.

CHAPTER VII

TERMINATION OF ATTACK. PROGNOSIS

Causes of Termination of Asthmatic Attack. —There are many possible explanations of the termination of asthmatic seizures, and presumably several are operative in each instance. As the therapeusis of asthma aims at the stimulation of the sympathetic system in order to overcome excessive parasympathetic activity, so we must look for the physiological development of this influence to explain the natural remission of the attack.

Now, sympathetic stimulation is brought about by oxygen want, the accumulation of carbon dioxide in the blood and anxiety. All three factors co-operate and increase in degree as the paroxysm proceeds and ultimately produce the necessary correction of nervous balance. Possibly their efficacy lies in an augmented secretion of adrenalin which is certainly enhanced by the violent muscular efforts at respiration.

The experimental injection of peptone or histamine into guinea-pigs produces bronchospasm, which is followed by relaxation for a considerable period, during which time further injections are without effect. Whether this loss of susceptibility and the ensuing refractory period to protein products occur in man is uncertain. As against this view can be ranged the multitude of sufferers whose asthma or hay-fever persists with trivial remissions until removed from the exciting causes.

Finally the experiments of Oeller and Schilling (*q.v.*) suggest that accumulation of eosinophils plays an important part in bringing an asthmatic attack to its close.

Prognosis.—The prognosis of bronchial asthma is one of the greatest difficulty. So far as longevity is concerned, the outlook is not necessarily adversely affected. Many asthmatics live to well past middle age, for they seem to be less prone to other diseases which are apt to arise in the fifth decade. Family longevity is a point to be borne in mind in regard to the future.

The age of onset has important bearing on these matters. Thus, if starting in infancy and persisting into adult life, it is clear that

organic changes will be more in evidence at middle age than if the asthma arose in the adult. On the other hand, if confronted with a child asthmatic the prognosis for recovery is often better than in later life because the asthmatic attacks may cease entirely at puberty. If a family history of asthma is forthcoming, then this happy event is unlikely to occur. The recovery at puberty is no doubt in part related to the alteration of endocrine balance which takes place, and in part to the increased stability of the nervous system in the adolescent as compared with that of the infant.

In women, asthma confined almost exclusively to the menstrual periods will probably remit at the menopause.

Asthma appearing for the first time at middle age will almost certainly persist throughout the remainder of the patient's life.

The presence of organic disease naturally renders the outlook less favourable. Thus emphysema and evidence of congestive failure not only denote the likelihood of the continuance of asthmatic attacks, but also forecast a shortened life. It should be remembered that both emphysema and cardiac decom-

pensation may be more apparent than real, however, for we have noted the difficulty of differentiating these states from those of over-distension of the lungs, which is still amenable to treatment, and venous congestion.

Chronic bronchitis is definitely unfavourable, for it not only tends to excite asthma, but also to produce emphysema and strain on the right side of the heart.

The length of the individual attacks is important because protracted seizures induce considerable pulmonary congestion, which therefore takes several days to clear up. The lungs are thus exposed to greater trauma and danger of intercurrent infection.

The frequency of attacks and the completeness of recovery between them must also be considered for similar reasons.

Enquiry should be made to ascertain whether the paroxysms are becoming more severe or more frequent as age advances. This is quite often the case, the unfortunate sufferer seldom being free day or night from the distressing symptoms of his malady. The loss of strength and appetite consequent to disturbed sleep and perpetual dyspnœa is

only too apt to accelerate the advent of the final breakdown.

If a definite exciting cause can be detected, the asthmatic's outlook is at once rendered more favourable. If, on the other hand, the patient show allergic reactions to numerous substances, the chances of cure are very remote.

Probably the most favourable type of the disease, excluding hay-asthma, is bronchitic asthma, for the patients are frequently spared during the warm months, and have time to recuperate, they respond to treatment, and if in the position to do so often escape the disease by wintering abroad.

Lyon and Murray-Lyon (18), in reviewing the results of treatment of asthma, emphasize the importance of treatment in the early years of the disease if a cure is to be attained. They conclude that cases arising in the first five years of life are less successful than those beginning later and suggest that this may depend on hereditary influence. They note also that asthma starting after middle life is usually less amenable to treatment.

CHAPTER VIII

PRELIMINARY INVESTIGATIONS

History.—It is of the utmost importance that a full and painstaking enquiry should be made into the history of the asthmatic patient. The knowledge gleaned therefrom must of necessity affect profoundly the choice of therapeutic measures to be adopted.

In the first place, the family history should be scrutinized, for the prevalence of asthma in near relatives will not only point to a guarded prognosis, but also to the likelihood of the disease being of the frankly allergic type. This in its turn will indicate the advisability of very complete biochemical, bacteriological and sensitization tests being performed.

The age of onset may be helpful in directing attention to the provocative of the attacks. Thus infantile asthma is almost always of the primary type, and the allergen is usually to be found in one of the common foods. Asthma arising in later life is more often due to hyper-

sensitivity towards animal or vegetable emanations or to bacteria.

The nature of the earliest attacks should be determined, because the account will be uninfluenced by experiences resulting from such complications as bronchitis. If there were true paroxysms, possibly ushered in by sneezing or profuse rhinorrhœa, but unassociated with any respiratory disease, allergism is indicated. If, on the other hand, there is a history of recurrent colds or bronchitis leading eventually to outbreaks of asthma, a bacterial cause must be sought.

Too much importance cannot be attached to other manifestations of allergic reactions. Thus infantile eczema, urticaria or cyclical vomiting give strong grounds for the supposition that the patient belongs to the first group.

The periodicity of the attacks should be carefully noted, more especially in relation to the first few years of the disease. Winter asthma is in many instances immediately related to infections of the respiratory tract, whereas that occurring in the summer is often caused by pollen or seasonal fruit. Nocturnal attacks, though by no means limited to any one type of asthma, should stimulate searching

enquiry into the quantity and quality of food taken in the later part of the day. Or again, the paroxysms may be induced by the presence of a specific allergen in the bedding, e.g. moulds, feathers, etc. In this case it may be found that no attacks have occurred when sleeping in other houses, or on a new mattress, and so on. Weekly seizures strongly indicate dietetic indiscretions. Particularly in children is it found that on Saturday or Sunday night they are permitted to stay up later than is their wont, and to partake of a full evening meal. Asthma occurs in the small hours of the next morning, and may be eradicated if the patient be warned off eating after the late afternoon.

Attacks occurring at the menstrual periods will occasion an examination of the pelvic organs to determine the presence of any abnormality whose reflex effect would be enhanced by pre-menstrual congestion, e.g. a chronically inflamed appendix or Fallopian tube. In the absence of any deviation from the normal it is probable that the source of irritation falls into the endocrine group. The biochemical behaviour of the patient should then be investigated in the intermen-

strual and menstrual period. A marked fall of blood calcium may occur at the latter time, and correction of the deficiency may favourably affect the course of the disease. The prognosis here is more favourable than in many types, because of the tendency to recovery at the menopause.

Daily attacks should raise suspicions of organic disease which gives rise to repeated irritation of the respiratory tract.

The localities in which asthma is usually experienced and those in which it never occurs should always be determined. Actually it is difficult to draw conclusions as regards exciting causes from such data, because most asthmatics tend to be free from attacks for a variable time after each move. If their stay in the new place is sufficiently prolonged, the attacks usually return with all their previous vigour. However, bearing this in mind, one may yet again help by this question of locality. Thus prolonged residence in cities may be associated with complete freedom from asthma, whilst a visit to the country invariably spells a fresh outburst of symptoms. The larger the city and the more centrally situated the patient, the less likely is he to suffer, a fact which

suggests sensitiveness to tree or grass pollen, but in many of these cases no specific hypersensitivity can be demonstrated. On the other hand, some patients are always worse if living in a town, particularly in foggy weather. It is well to suspect an underlying bronchitis or sinus infection in such instances.

Asthma occurring in certain houses and never in others should always stimulate a vigorous search for a possible connection with objects such as cats, dogs, special bedding and so on which are recognized as relatively common sources of allergens. If these attacks occur only at night, special attention should be directed to any differences in meal times in the houses, to the nature of the bedding and to the composition of the bedroom dust. The importance of house dust may be appreciable, particularly in certain damp areas where fungi abound.

The nature of the patient's occupation may present a helpful clue, provided that the asthma first manifested itself after he had entered the trade. Familiar examples are those of a baker with intolerance for flour dust, or a chemist with susceptibility towards ipecacuanha, or a groom who is a "horse asthmatic."

Drug habits must be exposed more especially in relation to the antipyretic group such as acetyl-salicylic acid. Many people take this substance in the hope of aborting a cold, but attribute their asthma to the respiratory infection, and rarely volunteer any information in respect of the means they have employed to cure themselves.

The ill effects of certain animal emanations are seldom appreciated by the sufferer. The author has recently seen a patient a prey to asthma for ten years who has now been free for eighteen months as the result of ridding his house of a pet cat. He failed to grasp the significance of his freedom from trouble during the few weeks which intervened between the death of his first cat and its replacement.

Noxious articles of diet are on the contrary usually recognized by the patient and avoided. This statement is not meant to include all those foods which give positive skin reactions in asthmatic subjects, for many of these cannot be proved to be responsible for the attacks in so far as their exclusion often completely fails to alleviate the disease.

If the patient has observed no relationship between environmental conditions and the

occurrence of asthma, the exciting factor is probably of intrinsic origin. This indicates the necessity for a careful search for localized infection or sources of reflex irritation, such as constipation, intranasal deformities and the like.

Physical Examination.—The value of a careful clinical overhaul is twofold. In the first place, it may disclose abnormalities which are directly responsible for the asthmatic attacks. More commonly it reveals structural changes in the circulatory and respiratory systems on the recognition of which prognosis so largely depends.

Points demanding special attention are the state of the nose and throat and the condition of the thoracic wall and its contents. To find an anatomically perfect nose is extremely rare, and variations such as deflection of the septum, though worthy of note, should never give rise to great hopes of having discovered an important pathological feature. Of greater moment, however, is the presence of infected sinuses, more especially the ethmoidal air cells, and the existence of œdematous polypi blocking the naso-pharynx.

If the history gives rise to suspicion of a

catarrhal origin of the asthma, the accessory sinuses should be X-rayed.

The condition of the chest wall must be inspected to determine the degree of kyphosis and the extent to which this can be made to disappear on extension of the spine. The pliability of the thorax is a most important matter, as we have already noticed. It should be observed not only throughout the phases of respiration, but also during movements of the trunk, such as stooping, twisting and lateral flexion.

The lungs must be examined and note made of the respiratory excursion in quiet and forced breathing. Evidence of bronchitis and emphysema should, of course, be sought for, remembering that the clinical signs of the latter condition usually exaggerate the amount of actual damage which has taken place.

To estimate the degree of damage, if any, to the heart is extraordinarily difficult, because a rapid pulse, poor exercise tolerance, cyanosis and dyspnœa may all arise from co-existing emphysema. By the time that obvious signs of congestive failure occur, the condition of the patient is parlous and appreciable at a glance. In the absence of an independent

cardiac disease it may be accepted that organic changes in the heart are not likely to be present save in long-standing cases of asthma with complicating emphysema and chronic bronchitis. To judge accurately the size of the heart is seldom possible without the aid of radioscopy, because the hyper-resonant enlarged lungs render the practice of percussion an art more dependent upon faith than skill.

The condition of the peripheral arteries is of considerable significance from the point of view of prognosis. Arteriosclerosis occurs on the average at an earlier age in the asthmatic than in the normal individual and when widespread tends to produce, or is usually accompanied by, considerable loss of weight and lowered resistance towards catarrhal infections. Once it has become generalized, recovery from asthma is almost unknown.

Special Tests.—It must not be thought that all the tests to be mentioned need be carried out in every case of asthma. The history should give important clues for the detection of the type of patient with whom we have to deal and the probable sources of provocative factors. The method of so utilizing the

history has been explained, so with these reservations the various tests of value will be considered.

The Ether Reaction. — This reaction was described by Oriel (25) as one occurring in a number of diverse conditions, including those of allergic nature when in a state of activity. A little 25 per cent. sulphuric acid is added to the urine and a layer of ether is superimposed. The mixture, having been shaken, is allowed to stand. A positive reaction is indicated when the lower part of the ether froth becomes viscous. The degree of viscosity and the depth of this waxy scum determine the positiveness of the reaction. When strongly positive, the test-tube can be inverted without spilling. From such a urine a substance can be separated by precipitation with excess of alcohol. It is soluble in water and gives the ether reaction when dissolved in this medium. This body appears to be a proteose which in asthmatics produces the effects which we have already described. It will be remembered that it occurs in the frankly allergic type of asthma only and, therefore, this test need not be undertaken unless the history suggest that the patient belong to this class.

Fæcal Examination.—Examination of the fæces for the presence of imperfectly digested foodstuffs and abnormal bacteria should be undertaken if the history points to a relationship between digestive disturbances, certain foods, or constipation and attacks of asthma. The investigation is particularly important if a positive ether reaction has been obtained, for it is conceivable that the proteose is derived from protein cleavage products in the gut which are commonly closely linked with the presence of late-lactose fermenting bacilli. Flora of this type, the ether reaction and hypochlorhydria form a triad with considerable frequency in asthmatics of the first type.

Fractional Test Meals.—The indications for this investigation are those referred to in the first and second tests. The practical value of the results is, however, very small, because hypochlorhydria is by no means a constant finding in either group of asthmatic. In fact, the highest degree of hypochlorhydria the author has ever noted was found in a pollen-sensitive asthmatic of classical allergic type. It is probable that many instances of hypochlorhydria are in reality but cases of chronic

gastritis in which there is no fundamental defect in the formation of the hydrochloric acid, the substance being masked by excess of mucus present.

Examination of the Blood.—In an earlier chapter common deviations from the normal blood composition have been described, but only three of these need be sought for as likely to influence the course of treatment. These are the Van den Bergh reaction, the sugar variations and the calcium content. Here again, the examinations, especially the first two, are rarely called for in the patients of the second, or respiratory group. They should be performed on blood taken during or immediately after the asthmatic attack and again, if possible, in an inter-paroxysmal interval for the sake of comparison.

Sputum.—It is quite exceptional for a detailed examination of the sputum to be needed for aid in diagnosis. A bacteriological analysis is, however, most helpful to the treatment of asthmatics whose attacks are closely associated with disease of the respiratory system such as bronchitis. Infections of the entire respiratory tract may be responsible for repeated seizures either by reflex stimu-

lation or by the production of hypersensitiveness to bacterial products, and there can be no doubt that an autogenous vaccine often produces a remarkable amelioration of the disease.

Skin Tests.—The principle of these tests is that a specific allergen, when introduced into the skin of a sensitive individual, will produce a reaction in the form of a raised, red wheal sending out branches like pseudopods in all directions. The whole is surrounded by an erythematous zone. The size of the wheal, which may be an inch or even more in diameter, must be compared with that resulting from a control inoculation with the allergen solvent only. Except in cases of dermatographism, it is seldom difficult to convince oneself of the presence or absence of a positive reaction. In cases of doubt, the probability is against the tested substance being the exciting allergen.

Two methods of application are employed. The first is the scratch method in which the cleaned anterior surface of the forearm is cut at points one inch apart, each incision being about one-eighth of an inch in length. It is important that the scratch should be suffi-

ciently deep to open the superficial lymphatics, but not deep enough to cause bleeding. Considerable practice is, therefore, required before the test can be carried out expeditiously and accurately.

By exerting traction on the skin, the edges of the cuts are made to gape, and are covered with a drop of decinormal sodium hydroxide solution. A little powdered allergen is then gently mixed with the caustic soda solution which dissolves it. The arm is left exposed to the air for a quarter of an hour and thereafter any remaining solution which has not dried may be removed by separate pledgets of wool.

It is essential that contamination of one test point by material used on an earlier scratch should be guarded against, otherwise the experiment is invalidated. A chart of the position of the scratches and the corresponding allergens should be made at the time to prevent subsequent confusion. A control scratch into which decinormal sodium hydroxide only is rubbed must always be made, for some individuals react quite briskly to the slight trauma and solvent alone.

When the reaction is positive, a surrounding

flush and itching are observed in about ten minutes and a well-formed wheal in half an hour.

If the history leads one to suspect an extrinsic origin of the allergen, e.g. grass pollen, foods, dusts, etc., as opposed to those of intrinsic source, e.g microbial infection, the skin tests are worthy of trial, a positive result being obtained in more than half of this class, provided that, if the scratch method prove negative, intradermal tests be applied.

It is, of course, impossible to test out all the possible allergens separately, but powdered group preparations of allied substances should be employed in the first instance. Thus, one group may consist of dust, fur, feather and orris root extracts; another of rye grass, Timothy grass and other pollens and so on. Naturally, here again the case history is of great assistance in enabling one to decide the group which should be investigated. If any one group gives a positive reaction, then its individual components must be tested separately in order to incriminate the offending member.

A large number of allergens are now on the market in the form of dry powder, and appear

to be fairly stable in this form. In certain cases, however, it may be necessary to prepare special material for testing. Cohen (27) emphasizes the importance of house dust and mattress dust as sources of allergens. He collects this material from different parts of the house by means of a vacuum cleaner, each fraction being caught in a paper bag, which is then removed and appropriately labelled. The samples can then be extracted with a suitable solution which is used for skin tests.

Assuming that the scratch tests are negative, the attempt to identify the offending substance should not be abandoned, but intradermal application must be carried out. A much larger percentage of positives is obtained in this way.

A solution of the suspected substance or group of substances is injected into the skin of the arm or forearm at points spaced as for the scratch method. Again a control must be used. A finely graduated tuberculin syringe, preferably fitted with an eccentric nozzle, is employed for the purpose in conjunction with a number 17 needle of interchangeable type. It is necessary to have several such

syringes which should be charged with solutions before the test is commenced. 0·05 c.cm. is then injected intradermally, and if this is correctly carried out a blanched area of epidermis will be raised above the surrounding skin.

Positive reactions occur rather earlier than in the scratch tests and are more pronounced in character.

The significance and ultimate therapeutic value of skin tests are yet debatable points. Doubtless many of those who decry their value have not been sufficiently alive to the necessity of discrimination between the two main types of asthmatic, the allergic, in whom skin tests are usually positive, and the secondary form, in which they are not. Again, reliance on the scratch test alone will lead to erroneous conclusions as to the frequency of positive reactions. The painstaking researches of Coke (28) and others into the whole subject of allergy and its relation to asthma and cutaneous tests cannot be lightly dismissed, and there can be no doubt that a genuinely positive skin test often indicates the nature of the harmful allergen and thereby leads in some cases to successful treatment.

It is equally certain, however, that an appreciable proportion of patients giving positive skin reactions to certain substances do not benefit when removed from their sphere of activity, or when attempts are made at desensitization by the injection of minute quantities of the allergen. Again, cutaneous tests may suggest hypersensitivity in one individual to such widely diverse substances that one hesitates to conclude that they, one and all, are responsible for asthmatic attacks.

Rackemann (29), Moos (13) and others have pointed out that positive skin reactions may persist for years in spite of the production of clinical cure of asthma and absence of symptoms even when in the presence of the supposedly offending substance. This suggests that they may represent a phase of past history rather than the state of a present illness.

Further doubt on the value of cutaneous tests is cast by Dixon, who refers to the fact that they may be positive in normal individuals. He continues that the reaction is a local axon reflex and is not produced if the part is first anæsthetized. This suggests to him that the reaction indicates hyperexcitability of

nerve endings only. Of course, even if this is so we are but referred back to the asthmatic diathesis exhibiting itself in yet another manner. It is, however, difficult to accept the axon reflex as an explanation of the pronounced wheal which may occur from contact with one and only one allergen. There can be little doubt, in face of Lewis's (32) recent work on the blood-vessels of the skin, that the cutaneous reaction is ultimately due to the production of histamine and indirectly to the reaction of antigen and atopic reagin. The author has furthermore obtained a pronounced reaction in the skin of a hay-fever subject by scratch application of Timothy grass pollen after the production of local anæsthesia.

Although skin reactions to pollens and foodstuffs can often be produced, it is decidedly rare to achieve this when using bacterial or mould extracts, even when strong evidence exists of the complicity of these organisms. Grove (31), studying dust asthmatics, was quite unable to obtain positive cutaneous tests to *Aspergillus fumigatus*, though this organism is widely held to be a potent cause of asthma.

It is probably correct to conclude that a strongly positive skin reaction usually indicates the substance which is normally a provocative of the asthmatic spasm. If, however, multiple reactions occur, the likelihood of isolating by their use specific allergens is very small. The response is then indicative of heightened sensibility of the nerve endings to diverse stimuli and is but part and parcel of the asthmatic constitution. Finally a negative reaction does not always imply that the suspected material is innocent of allergenic power.

In the case of children it is seldom practicable to perform skin tests because of the fear induced by scalpel or hypodermic needle. As, however, young asthmatics are commonly food-sensitive, the offending substances can be discovered by making a detailed note of the diet for the twenty-four hours which preceded the attack and comparing this with the food taken in asthma-free periods. If asthmatic attacks occur daily, the probability is that a common article of nourishment is causing the symptoms, and a diet of fruit, vegetables and meat should be given in the place of one including eggs, milk

and bread. In this way it may be possible by the process of exclusion to arrive at the allergen.

Before leaving the subject of food tests further reference must be made to Oriel and Barber's work (26) on the urinary proteose. They quote Manwaring's experiments, which go to show that liver damage plays a very important part in the production of anaphylactic changes. Exclusion of this organ from the circulation, on the other hand, inhibits the action of the antigen. It is concluded, therefore, that the symptoms of anaphylactic shock are due to the liberation of a substance (anaphylotoxin) which is produced in the liver and has a histamine-like action. Thus it seems probable that in allergic states such as asthma the symptoms are not directly referable to an interaction of allergen and body tissue, but rather to a tissue reaction to secondary products emerging from the original liver damage engendered by the primary antigen.

For instance, fish antigen may cause liver damage which results in the formation of one or more secondary antigens (anaphylotoxins), which in their turn pass into the circulation

and excite asthma, urticaria or eczema as the case may be.

As these writers point out, in so many allergic diseases no one specific cause can be found for the attack, yet the urinary proteose is highly specific. The author has seen an asthmatic attack precipitated by the intradermal injection of 0·075 c.cm. of a 1 in 1,000,000 solution of proteose, an effect which could scarcely be ascribed to non-specific action.

The evidence is therefore in favour of the proteose containing the antigen substance which, in view of Manwaring's experiments, we may conclude, arises as the result of liver damage by the allergen. That hepatic disturbance does, in fact, exist in the asthmatic has been amply demonstrated in the earlier description of the Van den Bergh and sugar tolerance tests.

The value of the skin test with a solution of proteose is in the first place the demonstration that an active antigen has been obtained, and secondly in the estimation of the optimum dosage for commencing treatment.

Barber and Oriel advise a preliminary scratch test with a 1 in 10,000 and 1 in 100,000

dilutions. If the former is faintly positive and the latter negative, an intradermal test with 0·025 c.cm. of 1 in 1,000,000 is advised. A faintly positive reaction indicates that this strength is a suitable one on which to start treatment.

CHAPTER IX

TREATMENT OF THE ASTHMATIC PAROXYSM

Historical.—Prior to the introduction of adrenalin for the treatment of an asthmatic attack, the means employed to cut short the seizure were unreliable, very varied and usually extremely disagreeable. Ipecacuanha, antimony, lobelia and tobacco were in common use and employed in quantities sufficient to produce nausea and even vomiting. Strong cigars or pipe tobacco were smoked until the head reeled, the skin became moist and cold, the pulse feeble and the patient was horribly nauseated. At this moment the dyspnœa would cease as if by magic, leaving the victim prostrated by the effect of the drug. If the asthmatic gained relief from tobacco, it was essential that he should never smoke for pleasure lest he developed tolerance to the nicotine.

All four substances owe their action to sympathetic stimulation. In the case of

ipecacuanha and antimony the effect is indirect through the adrenalinæmia which immediately precedes vomiting. The well-known signs of sweating, pallor, rapid pulse and dilated pupils which immediately precede emesis are evidence of the part played by sympathetic activity. In the case of lobelia and nicotine, the action is twofold; the noted effect of nausea being reinforced by direct stimulation of the sympathetic ganglia.

Salter (2) refers to the use of strong, hot coffee taken on an empty stomach as often of use in asthma, though at other times this preparation undoubtedly precipitates an attack. He ascribes its efficacy to the stimulation of the higher centres of cerebration, pointing out that a state of drowsiness is conducive to the onset of an attack. The known stimulating effect of caffeine on the medullary centres is a good reason against its indiscriminate use, however.

Strong, hot alcohol in the form of whisky or brandy was at one time much in favour, but had to be pushed to produce intoxication with depression of the vagal centre in order to be of any use. Nowadays it is sometimes helpful as an adjunct to adrenalin in cases in

which broncho-spasm tends to recur soon after the effect of epinephrine has passed off.

The inhalation of chloroform and of amyl nitrite was practised in emergencies. The effect of the former is no doubt due to the depression it produces of the respiratory centre. Chloroform acts rapidly, but the amelioration is usually transient. The site of action of amyl nitrite is the bronchial musculature which it relaxes. Here the action is more prone to completely arrest the spasm than is the case with chloroform. In fact, it is still used as a measure to promptly relieve distress whilst an injection of adrenalin is being prepared. Unpleasant symptoms, such as flushing of the face, dizziness and palpitation, may result from its use, but are never of serious import.

The explanation of the value of inhaling fumes of burning saltpetre lies in the fact that nitrites are thus produced. Asthma papers consist of blotting-paper steeped in 20 per cent. potassium nitrate solution and then dried. Strips of this paper are burned, giving rise to a pungent smoke which must be drawn into the lungs in order to obtain relief.

Stramonium was extensively employed in

the past and still is, in fact, incorporated in certain proprietary preparations sold for the relief of asthma. The seeds or leaves are ground up and smoked, one pipeful being, as a rule, sufficient to terminate a paroxysm. The value of stramonium, like that of belladonna, lies in its anti-spasmodic action, the tendency to cause relaxation of unstriped muscle being much greater when it is in an abnormal state of contraction.

Some patients find that a regular pipe of stramonium smoked at bedtime will keep them quite free from attacks.

Proprietary Preparations.—The majority of asthma powders consist of a combination of saltpetre, lobelia and stramonium. The great objection to the regular use of any of these preparations which must be burned is that temporary relief is gained to the detriment of the bronchial mucous membrane, which is irritated by particles of soot and rendered liable to develop a state of chronic congestion in consequence. It is a fact (Hurst) that the users of proprietary powders suffer from a rapid increase in the frequency of their attacks.

A popular and well-advertised "cure" for asthma consists of cocaine, atropine and

sodium nitrite as the active ingredients of the solution which is sprayed into the nose. The combination is usually effective, cocaine stimulating the sympathetic system, atropine inhibiting vagal impulses, whilst the nitrite radicles produce relaxation of plain muscle. The objection to the habitual use of such powerful drugs by sufferers from a chronic disease is too obvious to require further comment.

Modern Methods.—An enormous advance in the treatment of the asthmatic attack was marked by the introduction of adrenalin. Reference has already been made to the rôle which this substance plays in the spontaneous relaxation of the bronchi at the close of a paroxysm. Its action is due to stimulation of the sympathetic terminals, thereby restoring the balance between sympathetic and parasympathetic influence. The rapidity of effect is one of its great advantages, for although local vaso-constriction is produced at the point of injection, sufficient is absorbed in a few minutes to counteract the excessive vagal activity.

Three to five minims of a 1 in 1,000 solution of adrenalin hydrochloride should be injected

subcutaneously, larger single doses being inadvisable. Over-dosage does not enhance the action of this substance, but is apt to give rise to unpleasant symptoms, such as palpitation, trembling and headache.

A minority of patients fails to respond to a single injection, and for these Hurst advises repetition of small doses every ten minutes or so until the broncho-spasm has yielded. The hypodermic needle should be left in place and 2 minims of adrenalin injected at frequent intervals, such as suggested above. The author has found this method extremely efficacious when dealing with an obstinate paroxysm.

Theoretically atropine should be of great benefit by depressing the endings of the vagus and thus again re-establishing the sympathetic parasympathetic balance, but in a different manner from that of adrenalin. The effect of the alkaloid is probably rather more complex than this, for it is known to allay abnormal muscle spasm without interfering with the passage of impulses from the controlling nerves, provided that large doses are not used.

Actually atropine does benefit the asthmatic and is useful as an adjuvant to adrenalin,

because the latter substance has but a short-lived effect, following which the paroxysm may return, though this is not often the case.

Atropine sulphate should therefore be given in doses of $\frac{1}{100}$ grain to $\frac{1}{60}$ grain. It is not completely excreted for several hours.

It should be borne in mind that an appreciable number of persons exhibit an idiosyncrasy towards the drug, and alarming symptoms may develop after the use of a small dose.

Of recent years ephedrine has come to the fore in the treatment of asthma. This drug is an alkaloid obtained from the Chinese plant Ma Huang, and has the pharmacological action of adrenalin, over which it possesses certain advantages.

In the first place, ephedrine, or the synthetic ephetonin, is effective if taken by mouth. It is very stable, and can be boiled without fear of deterioration. Its action lasts from three to five hours, the commencement being indicated by a rise of blood-pressure (33).

On the other hand, ephedrine is relatively slow to take effect, about half an hour elapsing between the time of its administration *per os*, or ten minutes subcutaneously, and the first

evidence of its activity. It is probable that its chief use will lie in the prevention of attacks in those asthmatics in whom periodicity is a noteworthy feature. Thus for the nocturnal type one grain taken at bedtime may suffice to ensure a peaceful night, whereas for patients subject to frequent attacks in the day and night half-grain doses every five hours may keep them free.

Daily repeated doses over a period of three or four months are worth trying in severe cases, because attacks recurring at frequent intervals can be accounted for in part as having assumed the character of conditioned reflexes. If the habit be broken in the manner suggested, the conditioned reflex will be lost. There is, however, some evidence that tolerance can be developed towards the alkaloid, in which case a prolonged course may prove to be ineffective.

Some patients experience unpleasant symptoms, such as palpitation, giddiness, headache and tinnitus, after the use of ephedrine, even in small doses.

Saussurea lappa, or Kuth root, an Indian shrub, contains in the root a substance or substances having considerable effect in cutting short a paroxysm. The root contains 0·5 per

cent. of an essential oil which is probably the active constituent, together with traces of an alkaloid, glucoside and resin. Chopra (34) states that the oil is rapidly absorbed and excreted through the lungs, producing bronchial relaxation and expectoration. Kuth root extract has also a sedative action on the central nervous system and promotes sleep thereby.

It is in no sense a cure for asthma, but merely relieves spasm and, if taken regularly, prevents the onset of further attacks. Chopra recommends the use of the following mixture :

℞	Pot. iod.	gr. x
	Tr. bellad.	♏v
	Sod. biborat.	gr.ij
	Extr. Saussur. lapp. liq.	ʒss. to ij
	Spr. chloroform	♏x
	Aq.	ad. ℥i

Sig. : ℥j t.d.s. et o.n. ex aq.

The treatment of an asthmatic attack should not stop at the administration of one or more of the above drugs. Although this alone will probably suffice to quell the paroxysm, yet the symptoms may recur as soon as the action has passed off. It is therefore essential to look for exciting causes and remove them. In the first place, the air of the room must be changed in order to rid the atmosphere of the

irritating fumes of an asthma powder which usually greet us on entry.

The patient should be placed in the best position to aid breathing, namely, sitting near a high table on which a pillow is placed to provide support for the arms. Pet animals and flowers must be removed from the room.

When the acute attack has subsided, questioning may elicit a history of constipation and a recent heavy meal. If this be the case, if recurrence of the attack is to be warded off, the stomach must be emptied by emetic or tube, and the bowels by means of an enema.

It is a good plan to leave the patient with a mixture of fifteen grains each of chloral and bromide, which should be taken if sleep does not supervene within a quarter of an hour.

Opium and opium derivatives should not be used except when absolutely necessary. Occasions do arise when morphine alone produces amelioration of an intense and agonizing paroxysm. The danger of morphinism in a disease of chronic nature must, however, be constantly borne in mind.

Of recent years various forms of inhalation apparatus[1] have been devised to supply the

[1] Of these, the Apneu apparatus is the best.

asthmatic with antispasmodic drugs in a state of fine division. Oxygen is passed through a solution of the chosen medicament, which is then reduced to a vapour of remarkable tenuity. Inhalation of vaporized adrenalin and stramonium brings an attack to a standstill almost immediately, and aborts a threatening seizure.

The great advantage which this possesses over such preparations as asthma powders and cigarettes is that there is nothing irritating in the inhaled material. The use of oxygen as a vehicle is far more efficacious than that of compressed air, owing perhaps to the relief of the excessive oxygen unsaturation of the blood which we have observed to exist in the asthmatic attack. Diminution of the excitability of the respiratory centre is thus induced.

Camps (35) in a recent article on the subject has stressed the unquestionable relief obtained by chronic sufferers, an opinion with which the author fully concurs.

One has been greatly impressed by the enthusiasm with which chronic asthmatics speak of this treatment as compared with all the usual forms of therapy. Not only do they find that attacks may be aborted by its

use, but also they notice a decided diminution in the frequency of paroxysms.

The patient must have the apparatus by the bedside for immediate use when an attack threatens. By regular employment of inhalation therapy, the asthmatic habit is broken and the tendency to further attacks is definitely reduced.

This form of treatment is particularly valuable for chronic asthmatics with bronchitis and emphysema, for which conditions creosote vapour should be inhaled twice daily on occasions when the asthma is quiescent. Should a paroxysm occur, adrenalin must be promptly substituted.

CHAPTER X

TREATMENT OF THE ASTHMATIC

The inter-paroxysmal intervals must be employed in an attempt to elucidate the nature of the provocative of the patients' symptoms. The result of the investigations will point to the most hopeful lines of treatment. Many of these are clearly only applicable to one particular type of asthmatic, whilst some are useful in the therapeusis of all sufferers. Bearing this in mind, the main principles of treatment will now be described without further reference to the types of asthmatic for which they are peculiarly suitable.

Removal of Exciting Factors: *Diet.*—A carefully regulated diet is an essential for all asthmatics, particularly in the direction of reduction of quantity and alteration of the times of meals. Dinner should be taken in the middle of the day; thereafter tea consisting of weak tea, bread and butter and fruit taken not later than 5 p.m. should constitute

the last meal of the day. Breakfast may be ample and include any food unless one or more has been proved to be a specific allergen.

For the majority of asthmatics it is wise to reduce protein intake, as will be readily appreciated on reference to the section dealing with biochemical abnormalities. It is well to enjoin abstention from meat except for one or two days in the week for all except children and adolescents. Naturally, if no benefit accrues from the observance of these restrictions over a period of two months they should be removed, for it must always be remembered that a considerable part of the treatment of asthma is still based on the principle of "hit or miss," in spite of the ever-increasing scientific knowledge of the disease.

If the patient has been shown to be sensitive to any one sort of food, e.g. egg or milk, the greatest care must be taken to exclude it from the dietary, even in minute quantities, such as may be used in the preparation of composite articles, e.g. cakes, bread and so forth. Should the patient have the misfortune to be sensitive towards a common article of diet, the difficulties of preventing

contact are at times almost insuperable, and demand efforts at desensitization.

Unless a definite provocative, alcohol may be taken in the form of lager, bitters or light wines. Sherry, port, cocktails and spirits are forbidden. A tumblerful of hot water should be taken before meals, because when taken in this way it leaves the stomach with great rapidity and, therefore, does not dilute the gastric juice when the food is taken. Furthermore, water taken on an empty stomach has been shown to reach the colon in a few minutes and, if taken liberally, effects a material reduction of the intestinal flora.

Digestive Disturbances.—The frequency of association of hypochlorhydria with evidence of imperfect protein digestion and hepatic derangement indicates the use of hydrochloric acid and pepsin in such cases. Sometimes a striking amelioration of symptoms is induced by the exhibition of the following mixture:

℞	Ac. HCl. dil.	♏ xv
	Pepsin	gr. ij
	Liq. strychnin. hydrochlor.	♏ v
	Syr. limonis.	♏ xx
	Aq. ad.	℥ ij

Sig.: ℥ ij ex aq. ℥ j t.d.s. cum cib.

Although it may be true that such a dose of the diluted acid produces no obvious change in the curve of the fractional test meal, yet it is equally certain that it is capable of relieving symptoms clearly referable to acid deficiency, e.g. achlorhydric diarrhœa.

The advantage of adding strychnine is that the alkaloid acts as a mild stimulant to peristalsis and overcomes the constipation to which many asthmatics are prone. There is no clinical evidence that in small doses it increases the excitability of the vagus centre.

Habitual constipation is best dealt with by means of suitable dieting, e.g. plenty of fruit, fruit juice, wholemeal bread and Bemax, abdominal exercises and massage, and copious water drinking. Liquid paraffin should not be given to the asthmatic, because it often produces flatulent dyspepsia, is nauseating and interferes with the digestion and absorption of food. Brisk purgatives must not be used habitually, as they are liable to further the absorption of imperfectly digested protein. If a laxative be required, sulphur or phenolphthalein are the substances of choice.

An exception to the rule is the asthmatic

who is warned of the approach of a seizure by an unpleasant taste in the mouth, drowsiness and abdominal distension. Here a timely half-grain dose of calomel may prevent the threatened attack.

Animal and Vegetable Emanations.—The extraordinary degree of susceptibility of certain asthmatics to various animals and plants has already been commented upon. When a clear-cut relationship between exposure to these influences and asthmatic attacks can be demonstrated, the prognosis is very favourable, provided that it be possible to prevent the patient from coming into contact with them. Thus many persons suffer from hay-fever and asthma only during the season of pollination, and may escape attacks if they spend these weeks in residence in the centre of a large town or more certainly if they go for a sea voyage. It may be noted here that pollen asthma is frequently outgrown, the attacks becoming progressively less frequent after the age of forty-five.

The matter is much more difficult for patients susceptible to emanations from domestic pet animals. Not only must they exclude such creatures from their homes, but

also they must exercise care lest they enter the house of a friend in which they are kept. The actual presence of the animal is not necessary for the precipitation of an attack; the mere proximity of, for instance, a dog basket may suffice to provoke a spasm in a suitable case.

Large cities are becoming progressively more advantageous for the residence of asthmatics of this group on account of the steady diminution of animal life in these areas.

The effect on the asthmatic of an atmosphere freed from allergens has been the subject of special study by Storm van Leeuwen (36) who found that in Holland asthma occurred with much greater frequency in districts of low altitude, especially if associated with a high degree of humidity, than at high altitudes. This fact he attributed to the presence of moulds or their spores, products of disintegration of insects and so forth, in the air and accordingly devised dust-free chambers for the use of the asthmatic. Such a room is supplied with air drawn from a height and warmed before ingress.

Patients commence treatment by living entirely in these chambers, and when they

have been free from symptoms for a few days they are permitted to go out-of-doors in the day-time, but must return to sleep in the allergen-free room at night.

Although it has been confirmed that such measures do result in great amelioration of the asthmatics' symptoms, yet it is clear that their value must be limited to a certain type of sufferer. Furthermore, the installation of dust-free rooms in private dwellings is associated with considerable expense, which for many would prove prohibitive. The author quoted advises the simultaneous attempt at desensitization with extract of various dusts.

Reference has already been made to the importance of considering the possible effect of house dust and that of bedding in particular. A change from an old to a new mattress may result in disappearance of nocturnal asthma for many months. The fact that recurrence usually takes place within a year suggests that the causative factor is the presence of a mould growing in the stuffing. If the mattress be covered over with a waterproof sheet the attacks will again abate.

The substitution of a flock pillow for the feather-filled article may again produce in-

stantaneous benefit in a patient susceptible to feathers.

The absence of luxurious bedding, dust and rich foods no doubt accounts for the well-known fact that the majority of asthmatics lose their symptoms on entry into hospital. The psychological effect of a large institution also plays a considerable part, however.

The effect of environment is not wholly a matter of the presence of allergens. Whereas Storm van Leeuwen attributes the benefit derived from residence at high altitudes to the absence of "climatic-allergens," Hurst rightly points out that this cannot always be the case. He notes the fact that asthma is practically unknown at altitudes of 4,500 to 6,500 feet, yet the Alpine huts must be favourable breeding-grounds for many types of dust-allergen. In furtherance of this observation, Hurst and Oriel (1) investigated the biochemical behaviour of an asthmatic at Villars (4,500 feet). They found that normal readings were obtained at this place, whereas a day later when in Paris a disturbance of the acid-base equilibrium was already noticeable, and was yet further accentuated on the second day, when the asthmatic reached London. Evi-

dently, then, altitude has a definite effect upon the biochemical behaviour of the asthmatic. That this does not depend upon the absence of allergens is shown by a further experiment by Hurst. He found that an asthmatic in whom an attack could invariably be precipitated by a minute dose of an autogenous vaccine could tolerate three full doses in the Swiss Alps with impunity.

Why it is that high altitudes should have so remarkable an effect on the patients' metabolism has yet to be answered.

Sources of Reflex Irritation.—Excluding chronic infection of the bronchi and such transitory sources of irritation as constipation and distension of the stomach, we find that the only area which is commonly associated with asthmatic paroxysms is that of the nose and throat. The importance of the upper and posterior part of the nasal septum as an excitatory region has already been noted, and this fact no doubt accounts for the appreciable number of patients who show improvement after pathological conditions here have been removed.

On the other hand, a cure of asthma is but rarely achieved by nasal operations, and it is

probable that much of the improvement noted is due to the removal of one site of peripheral irritation which happens to be particularly potent in the production of broncho-spasm.

Operative interference should be advised in the presence of definite localized sepsis or of equally definite obstruction to nasal breathing. Thus it is clear that pus in the ethmoid air cells or maxillary antra demands energetic treatment. Again, nasal polypi, which almost invariably denote infection in this area, are prone to aggravate the asthmatic symptoms by direct obstruction and by reflex irritation. They should therefore be removed. But when it comes to the consideration of a deflected septum, a well-balanced judgment is a necessity if our patients are to be spared unnecessary operations. The mere deflection of a nasal septum is so common that it might indeed be regarded as the normal for the northern races. In spite of this we find certain specialists advocating submucous resection on the slightest provocation. Failure to cure is then explained as being referable to insufficient removal of the bony portion, and a further operation is advised. It is the general practitioner, not the operator, who sees the unfavour-

able results of such operations, in the nature of nasal discharge, crusts, recurrent colds and sore throats.

An immense amount of harm may be done by this operation alone and should never be advised without the most careful consideration of the local and general condition. If it be decided to carry it out, it is essential that it should be performed by an expert surgeon of wide experience, for the after results will depend largely on his knowledge of when to stay his hand.

Marked septal deflection sufficient to obstruct breathing and to bring the septum and middle turbinal into contact, permanently or at times of congestion, should be corrected. In the first place, such a state of affairs must give rise to pathological stimulation of the spasmogenic area of the septum.

Secondly, the obstructed air-way leads to mouth breathing, especially at night when the patient is asleep. This in its turn produces sore throat and aggravates any existing bronchitis.

Thirdly, repeated colds affect these individuals ; clearly an undesirable element in the life of an asthmatic.

Similar considerations should act as guides when contemplating turbinectomy.

A permanent decrease of asthmatic attacks seldom, if ever, follows the removal of infected tonsils or teeth. As regards the latter, an exception must be made in cases of " open " sepsis combined with bronchitic asthma. The eradication of pyorrhœa will then cause an improvement in the bronchitis and an appreciable amelioration of asthma.

When operation is genuinely indicated by pathological conditions of the upper respiratory tract, then its performance will result in improvement in the patients' condition in slightly over 50 per cent. of cases. By improvement is meant a reduction of the frequency or intensity of asthmatic symptoms.

The number of cases cured according to recent statistics (18) is less than 20 per cent. On the other hand, these figures include such operations as tonsillectomy, which are useless *qua* asthma, and give, therefore, an unduly pessimistic outlook on nose and throat surgery for this condition.

In an earlier part of this work we have discussed the value of cauterization of the sensitive area of the nasal septum. This

procedure holds out the greatest hope of relief in cases in whom rhinorrhœa or sneezing precedes the paroxysm (hay-fever excluded), and where contact is made between the middle turbinal and septum. Temporary improvement following cauterization is common: permanent benefit is very rare.

Various local applications to the spasmogenic area have been advised in order to avoid operative interference. Dundas-Grant favours the following:

℞	Anæsthesine	grs. xx
	Vaseline	ʒij
	Adrenalin	♏xx
	Paraf. liq.	ʒij

Psychotherapy.—The extravagant claims which have been made for the value of psychotherapy in the treatment of asthma would fill one with amazement were it not for the fact that many asthmatics are of neurotic temperament and family history. Furthermore, most practitioners will have encountered cases in which the onset of a paroxysm coincided with emotional stress engendered, for instance, by the thwarting of a wish, or by the desire to escape from an awkward situation, and so forth. In hospital the appearance of the

house-physician on his night round may be sufficient to provoke an asthmatic paroxysm, sometimes in order to single out the patient from the rest of the ward as a centre of interest, at others in the hope of obtaining morphine. That with due precautions such attacks may be conquered by an injection of water has already been noted.

All that these and similar manifestations show us is that the vagal centre can be influenced by activity of higher levels of the brain, and, being inherently hypersensitive, is liable to express this influence in an asthmatic paroxysm. Psychical stimulation falls into line, therefore, with that which may originate from any other part of the body. The number of cases in which asthma can be regarded purely as a neurosis is decidedly small.

On the other hand, we have to recognize that the majority of chronic asthmatics are prone to attacks in which the nervous element appears to be the only existing excitant at the moment. The fear of a paroxysm or the sight of a place where an attack has previously occurred may be sufficient to precipitate it afresh, the asthma partaking of the nature of a conditioned reflex. Our patients should

therefore be made aware of this factor, and assisted by rational psychotherapy to help themselves to overcome it. One of the results of constant use of ephedrine or inhalation therapy is to break the habit—to destroy the conditioned reflex.

Moos (13) claims great success from his psychotherapeutic efforts, but it should be borne in mind that the psychologist deals as a rule with picked cases selected by the general physician for his help.

He advises daily sittings for six to eight weeks; at the end of this period the majority are stated to have improved enormously. At the completion of treatment the signs of bronchitis and over-distension have disappeared, the sputum has diminished and Charcot-Leyden crystals and Curschmann's spirals vanish rapidly, whilst the eosinophil cells return to normal numbers.

Moos advises that during treatment drugs should be gradually discontinued, but points out that this will be difficult of accomplishment unless the physician be constantly at hand so as to lend his moral support when a paroxysm threatens.

Hypnotism may be of use to cut short an

attack, provided that the patient has already been under psychological treatment for some time and is duly impressed by the personality and powers of the psychologist.

The asthmatic is taught to seek for the mental causes of each attack, and eventually becomes so proficient that he recognizes these almost as they arise, and therefore suffers less and less.

Moos explains the frequency of nocturnal attacks as expressive of dreams of unfulfillable desires. He states that skin reactions to proven allergens fail to appear after adequate psychotherapy, and suggests that sensibility to these substances can be increased or inhibited by the state of a patient's mind.

There is no greater danger to the asthmatic than that of falling into the hands of a specialist in the first instance. By the very nature of his self-imposed limitation the psychologist or nasal surgeon is apt to have a warped sense of values. Although he is often indispensable for successful treatment of the asthmatic, yet the main control of the patient should always be left in the hands of the general physician. Were this the case, the progress towards the elimination of asthma would

suffer fewer set-backs resulting from misleading claims on behalf of specialized branches of therapeutics.

Spa Treatment.—The best-known spas at which special attention is given to asthmatics are Mont Dore, Aix-les-Bains and Allevard-les-Bains. Particularly at Mont Dore is systematized treatment carried out. Here baths, of which the vapour contains arsenic, massage and remedial exercises are given with strikingly good results. Such a locality is specially suitable for chronic asthmatics in whom the typical stance and chest deformity have been developed. The nature of the physical exercises aiming at reduction of this feature will be discussed subsequently in a section devoted to the subject. It is a pity that in England the undoubted value of spa and inhalation therapy is given such scant attention, for they are well worthy of study, as the greatest benefit is often derived from their use.

It is a good plan for patients who have completed their course at these resorts to spend a further month in the Swiss Alps, remembering the noted freedom from asthma at heights in the neighbourhood of 5,000 feet.

If emphysema is present, but bronchitis relatively slight, residence at this height is not contra-indicated. If, on the other hand, bronchitis is a prominent feature, high altitudes tend to produce exacerbations of the catarrh, and should be avoided.

Desensitization. (*a*) *Specific.*—It will be remembered that certain asthmatics can be shown, by skin and other tests, to be hypersensitive to some particular protein or drug which appears to be the usual provocative of their paroxysms.

We have dwelt on the subject of avoidance of such substances, but as in many cases this is not feasible, an attempt must be made to desensitize the patient by injection of minute quantities of the offending matter. Such a process is known as specific desensitization as opposed to non-specific treatment, in which the same result is aimed at by the injection of substances of protein nature which cannot be shown to be true allergens.

An illustrative example of the former method is the use of pollen vaccine for the hay-fever asthmatic. The author has obtained excellent results by the use of Pollaccine, and is of the opinion that many failures are due

to insufficient time devoted to the course of injections or to over-dosage.

A male whose life was wellnigh intolerable during the pollinating season on account of asthma had been treated by pollen vaccine for many years in succession without noticeable improvement. The following course of Pollaccine was then instituted, with the result that the subsequent summer was passed through with far fewer and milder attacks than had occurred heretofore. The course was repeated during the next winter and spring, with still further improvement, only one asthmatic attack, and insignificant sneezing and lachrymation, arising in the next season. It should be added that the patient gave a strikingly positive skin reaction to Timothy grass pollen, from which, by the way, Pollaccine is prepared. The course was as follows:

Every two days, commencing in early December, the patient received injections of Pollaccine. The initial strength was 50 units per c.cm. $\frac{1}{10}$ c.cm. (5 units) was injected intradermally for the first dose, each subsequent dose being raised by increments of approximately 25 per cent. of that which preceded. After the third injection the

quantity was reduced again to $\frac{1}{10}$ c.cm., but administered subcutaneously. This form of injection was used for all subsequent occasions until near the close of the course. When 1 c.cm. was reached, a solution containing 100 units per c.cm. was employed, the quantity to be injected being calculated on a percentage of the number of units of the prior dose. When eventually 1,000 units were being given without sign of reaction, the interval between injections was lengthened, so that the patient attended on two days a week only. Finally, in May of the following year to that in which treatment commenced, 1,000 units were given intramuscularly twice weekly to the end of the month. The course was then modified by giving 100 units twice weekly until the hay-fever season had definitely arrived, as decided by observation of controls (the commencement of the season varies yearly according to weather conditions).

It was interesting to note that whereas early in treatment the patient had a violent attack of hay-fever and asthma due to accidental over-dosage, yet towards its close he was receiving double the amount of Pollaccine and evinced no discomfort.

The same principles guide the attempts at desensitization of patients to egg-white, fish, horse-dander and so on.

In every case a positive skin reaction should be obtained, and an attack precipitated by the use of the substance in question. Having satisfied oneself on these points, it must be taken as a rule that benefit cannot be expected unless the course extends over many months, and unless the dosage is so carefully graduated that no further reactions are produced by treatment.

Success cannot be foretold by disappearance of the positive skin test. If the reaction can no longer be elicited, the outlook is good ; but if it persists the result may be equally good, a fact which shows the fallibility of these tests.

The great objection to specific desensitization is the length of time and expense involved, and the uncertainty of effect even if every precaution has been taken.

In the event of an attack of asthma being precipitated by an injection of allergen, prompt administration of 5 minims of adrenalin solution will abolish it with rapidity.

If it be true that the phenomena of asthma

and certain other allergic diseases depend in part upon the production of secondary antigens, as has been suggested (*q.v.*), the difficulty of efficient desensitization can be at once appreciated.

We are therefore led to enquire what effects are obtainable by the injection of graduated doses of the urinary proteose of Oriel, which appears to be specifically antigenic (26).

It has been stated that this substance will give positive skin tests in extreme dilutions (1 in 1,000,000), and call a paroxysm into being when administered in this dilution in such doses as 0·1 c.cm. By analogy one is led to hope that prolonged treatment with proteose will give results as good as, if not far superior to, those produced by, for example, pollen vaccine.

The work on this subject is too recent to justify anything savouring of finality in the reply to our self-imposed question; but evidence of the efficiency of proteose injections is accumulating.

The writer, though possessed as yet of limited experience of this treatment, is convinced of the necessity of exercising extreme caution in

the matter of dosage. In an earlier chapter the method of arriving at a suitable initial dose has been discussed, and it should be rigidly adhered to in every case. In a recent instance it was found that any attempt to raise the amount above 0·075 c.cm. of 1 in 1,000,000 dilution intradermally invariably resulted in an attack of asthma, whereas if this figure were not exceeded, the previously diurnal attacks occurred at ever-lengthening intervals.

Not only is one dealing with a substance far more potent allergically than any of the common protein preparations, but also one must bear in mind that the urinary proteose is not standardized ; is not, in fact, a chemically pure substance. It must therefore be tested out with caution on each patient from whom it has been recovered.

The advisability of combining the course of proteose injections with oral administration of glucose and ammonia will be discussed later.

(*b*) *Vaccines.*—The use of vaccines as a therapeutic measure hovers between the specific and non-specific desensitizing methods.

In view of the fact that anti-catarrhal vaccines have their chief value in the treatment of asthma superimposed upon infection of the

respiratory tract, it is probable that the action is a specific one.

Vaccine therapy has been employed so extensively in so many diseases with such disappointing results that one would hesitate before recommending it to the asthmatic were it not for the appreciable number of patients who have undoubtedly derived benefit from it.

The essential points to be borne in mind are that only those patients whose asthma appears to be clearly secondary to a catarrhal infection of the respiratory tract should be subjected to vaccine treatment.

Secondly, the course of injections must extend over several months, and commence at the season of the year when the seizures are least frequent. In this type it is generally the summer.

Thirdly, the dosage must be regulated by the response of the individual, i.e. if a constitutional reaction follows injection, the next dose must be smaller, and subsequent increments based on a lower percentage.

It is a mistake to aim at attaining the maximum dose suggested by the bacteriologist who has prepared the vaccine. Many patients can never reach this amount without suffering

from asthmatic attacks. One soon learns to recognize the danger limit for each individual, and should then give quantities just short of this for the remainder of the course.

It follows from this that a vaccine should be supplied in rubber-capped bottles and not in coloured ampoules, which are not only wasteful but invite penny-in-the-slot methods of administration.

Probably the best results are obtained by the use of a vaccine prepared from the patient's sputum, but the author has witnessed many instances of improvement following the employment of a stock preparation containing a mixed flora.

The vaccine actually employed has been "Anti-Catarrh Vaccine."[1] Each cubic centimetre is stated to contain 50 million each of M. catarrhalis, B. pneumoniæ, and B. septus; 250 million each of pneumococci and B. influenzæ; 25 million streptococci.

The initial dose should be $\frac{1}{10}$ c.cm., subsequent doses rising by 25 per cent. increments unless constitutional reactions indicate a modified procedure. When the maximum optimum

[1] Prepared for Messrs. Parke Davis & Co. at St. Mary's Laboratories.

quantity has been reached, this should be adhered to to the end of the course in the late spring.

As a rule injections should be given every five days until the full dose has been reached. The interval should then be made a week, and later two weeks.

This treatment must be carried out every year, though after the first two winters it can often be considerably curtailed.

Should an attack of acute bronchitis, coryza or influenza arise in the course of the treatment, injections should be suspended until recovery has taken place.

The next dose must then be reduced to at least half of that which preceded the acute infection.

The use of vaccines prepared from pus from infected sinuses appears to be useless. The cleaning-up of such foci either results in cessation of asthma, or diminution of the intensity and frequency of the symptoms, but inoculations have no further influence on the malady.

(*c*) *Non-Specific.*—The results of this method of attempted desensitization are on the whole disappointing.

Peptone.—Loeb (38) and others claim good

effects from the use of Witte peptone in 4 per cent. solution. He advises intramuscular injections two or three times weekly, starting with $\frac{1}{10}$ c.cm. and rising to 1 c.cm. Twelve to fifteen injections complete the course, which should be repeated twice yearly.

A more elaborate technique which the present writer has found of value in a few cases out of many who have been subjected to it consists of the intravenous administration of peptone solution. A 1 per cent. preparation is employed to start with, and of this the initial dose is 0·05 c.cm. Injections are given every third day, the quantity being determined on the principles already enunciated.

Intravenous peptone therapy is by no means free from danger. Purity of the product is essential, and the liability to contamination by micro-organisms demands the greatest care in handling the solution. Over-dosage may produce alarming symptoms.

Tuberculin.—Storm van Leeuwen introduced non-specific desensitization of asthmatics by the use of tuberculin. Encouraging results have been reported, but as this might be said of any new line of therapy for asthma, one must await the observations of many workers on a

large number of patients over a period of several years before accepting any conclusions on the matter.

The sensitiveness of the patient is first tested by an intradermal injection of $\frac{1}{10}$ c.cm. of a 1 in 1,000 dilution. A strongly positive reaction indicates an initial dose of $\frac{1}{10}$ c.cm. of 1 in 1,000,000 dilution of old tuberculin subcutaneously. The injections are repeated every two days, rising by 25 to 50 per cent., but after two weeks they are given at five-day intervals, and subsequently once a week. When the actual value to be injected reaches 1 c.cm., a stronger solution is employed, with corresponding reduction of dose.

For patients who show but a trivial reaction to the skin test, a 1 in 100,000 or 1 in 10,000 solution may be used from the start.

The treatment should extend over six months at least.

Storm van Leeuwen reports cures or great benefit in over 75 per cent. of cases subjected to tuberculin therapy.

Maxwell (39), reviewing the results on thirty-six patients eighteen months after tuberculin treatment, reports that seventeen had been completely free from attacks for at least a

year ; twelve had improved, and seven failed to improve.

He considers that the method is so simple and the results so promising that it is well worth a trial.

Diathermy.—Treatment by diathermy alone never results in cure of asthma, but it is a very useful adjunct to other therapeutic measures in those patients whose attacks originated from a respiratory infection.

Ghimus (40) advises the application of large electrodes to the chest and back for half an hour at each sitting. The number of attendances varies from fourteen to eighty.

He explains the beneficial results as being due to an antispasmodic effect on the pulmonary parasympathetic fibres, together with a direct action of the heat in aiding the resolution of inflammatory products left as the legacy of a pre-existing disease, e.g. pneumonia or influenza.

X-Ray Treatment.—This, like diathermy, should only be used when more rational lines of treatment fail. The beneficial effect of X-rays on certain asthmatics is not understood, the possibility of their use being suggested by an accidental improvement in

an asthmatic patient whose spleen was subjected to irradiation on account of co-existing leukæmia.

At first the spleen used to be selected for the application of the rays on the assumption that its radiation reduced the power of allergic response. More recently the rays have been directed to the lung roots, but for this technique the so-called "deep X-ray" therapy has the most frequent effect. In view of the fact that this Erlangen treatment is known to aid absorption of inflammatory products (compare the beneficial effect in certain cases of chronic arthritis (41)), it is to be expected that its chief value will lie in dealing with patients of the second, or respiratory type.

Ultra-Violet Rays.—The employment of various sources of ultra-violet radiation, e.g. sunlight, or mercury vapour, tungsten and carbon arc lamps, has, it is almost needless to state, been advocated for the treatment of asthmatic sufferers.

It seems that whatever benefit it confers will be seen at its best in young patients and not in the confirmed asthmatic.

The action is probably twofold. In the

first place, the tendency to recurrent catarrhs is undoubtedly reduced by a careful and prolonged course of general irradiation. This may depend upon the second factor, namely, the formation and liberation of vitamin D from the skin which is induced by the action of the rays. As a consequence there is stated (42) to be an increase of active calcium in the blood, particularly if this drug be administered simultaneously. In view of the variations of calcium metabolism quoted in the section dealing with biochemistry, a logical ground for the use of ultra-violet rays is thus exposed. By increasing the ionic calcium in the blood the irritability of the vagus will be reduced, and likewise the tendency to asthmatic attacks.

Medicinal Treatment. (*a*) *Calcium.*—It follows from the preceding paragraph that the oral administration of calcium is advisable if it be present in abnormally low percentage in the blood, or again if the active calcium is reduced even in the presence of a normal total.

E. C. Warner has shown that the simplest method of estimating the active blood calcium is to assess the total quantity of this substance present in the cerebrospinal fluid. The choroid plexus acts as a dialyzing membrane

and thus saves much trouble and expense on the part of the investigator.

The mere administration of calcium lactate by mouth is insufficient, however. In order to raise the active blood calcium, the exhibition *per os* of about 30 grains daily must be combined with ultra-violet radiation, or with the easier alternative of the consumption of irradiated ergosterol, e.g. radiostoleum or vigantol (42), in 10-minim doses twice daily.

(*b*) *Neopancarpine.*—Mattausch (43) writes favourably of this drug as a preventive of paroxysms, but it is doubtful whether an appreciable number of cases derives permanent benefit from its employment. Nevertheless, any measure which can keep asthma in check for several months on end is worthy of notice, not only because by so doing the development of organic changes is delayed, but also because of the value of breaking the asthma habit.

On theoretical grounds one would have thought that neopancarpine was the last drug one should give to an asthmatic. It consists of an ethereal hydro-alcoholic extract of jaborandi, and thus contains pilocarpine in addition to certain volatile oils and resins.

Vernet declares that instability of receptiveness of the sensory fibres of the vagus is the fundamental abnormality in the asthmatic diathesis and ascribes the value of neopancarpine to the stabilizing effect of this preparation on the nerve endings. The arguments in support of this view are far from convincing.

Prolonged treatment is advised, starting with 10 to 20 drops thrice daily in water after meals. Apparently it is important that the drug should be given soon after taking food, for it is apt to cause retching if taken on an empty stomach. On the other hand, sweating and salivation are regarded as favourable features. This suggests that the production of premonitory signs of nausea and vomiting may be the real explanation of the beneficial effect of the drug, just as ipecacuanha, tobacco and other preparations have been shown to be effective. Possibly the more complete extraction of jaborandi leaves accounts for the differences of action of pilocarpine and neopancarpine, the as yet unidentified by-extractives inhibiting the parasympathetic-stimulating activity of the alkaloid.

It should be borne in mind that pilocarpine

does not act exclusively on the cranio-sacral division of the autonomic nervous system. In man sympathetic stimulation may at times appear to be its chief action, palpitation, tachycardia and profuse sweating being produced by its administration. Again, the adrenalin output is increased by pilocarpine, so that the apparent paradox of jaborandi extract being used in treating asthmatics becomes capable of explanation.

Mattausch believes that neopancarpine is particularly useful to the asthmatics whose attacks depend upon a source of bronchial irritation.

(*c*) *Ephedrine.*—The possible value of prolonged treatment with ephedrine apart from its use at the commencement of an attack has been discussed in an earlier section.

The principle of its use in this manner is the same as that for neopancarpine.

(*d*) *Glucose and Ammonia.*—To appreciate the rationale of treatment of asthmatics by glucose and ammonia it is necessary to recall the biochemical deviations which have been quoted from Oriel and others (1, 24, 26).

It will be remembered that their investigations brought to light the interesting facts

that the allergic type of asthmatic during an attack showed well-marked evidence of liver damage, with low blood sugar, raised amino-acid content and increased excretion of ammonia in the urine, which is partly, at any rate, a response to existing acidosis. At the same time a substance of proteose nature is found in the urine.

The clinical use of glucose in certain allergic conditions in children has been advised for some years by Cameron (44) and Osman (5), who have remarked on the remarkable cure which this substance can effect in some types of juvenile asthma.

In view of Oriel's findings it appears that glucose owes its efficacy to increasing the store of liver glycogen.

The presence of adequate supplies of glycogen in the liver is essential for its anti-toxic function and for its proper performance in the processes of protein metabolism, e.g. the breaking-down of amino-acids. It must be clear that the necessity for the exercise of these functions to the fullest extent is highly desirable to the asthmatic.

Glycogen is known to disappear in large quantities from the liver in anaphylactic

shock, a fact that suggests that the liver cells make use of it in combating antigenic substances conveyed to them by the blood-stream.

Oriel and Barber (26) have made the significant observation that the proteose excreted while the patient was taking large quantities of glucose failed to give a skin reaction, but that it was obtained from his proteose after dextrose had been omitted for some time.

Pure powdered glucose should be given in quantities of four ounces daily for the adult. This quantity is administered in divided doses in a tumblerful of water on rising, at midday and at bedtime.

Ammonia in the form of sal volatile, which, it will be remembered, consists of ammonia, ammonium carbonate and volatile oils dissolved in alcohol, has been recommended by Oriel (25). The idea arose from the observation of the increased ammonia excretion and acidosis. In the allergic type of asthma it certainly does produce remarkable results at times, especially if combined with glucose treatment. Apart from other effects, the administration of ammonia aids in the conversion of amino-acids into urea, whilst the

drug itself likewise undergoes this transformation.

In adults half a teaspoonful in water is taken thrice daily before meals. A few patients declare that it gives them indigestion, but the majority tolerate it quite well.

Treatment by Physical Exercises and Massage.—No branch of therapeutics is at once so valuable and yet so little employed as that of physical treatment of the asthmatic.

There is no point in prescribing this for patients who have but occasional attacks separated by long intervals and who therefore present none of the characteristic attitudes of the habitual sufferer. All other asthmatics, including those with chronic bronchitis, should be subjected to physical treatment as a matter of course.

The necessity of it will be made clear on reconsideration of the postural and pulmonary changes induced by asthmatic attacks. It will be remembered that the patient, even in the interparoxysmal intervals, holds himself tensely and rigidly, is unable to relax and perpetuates the thoracic displacement of the active disease into the quiescent intervals.

The lungs, in like manner following the

movement of the chest wall, remain constantly distended.

The duty of the masseuse is to restore mobility and flexibility to the thoracic parietes ; to teach the patient general muscular relaxation ; to guide his respiratory movements with a view to re-establishing a normal rhythm ; to assist in the expulsion of air from the pulmonary alveoli ; and finally to apply massage to the limbs in order to aid the venous circulation and prepare the body for active exercises.

Various schemes of exercises have been advised by several workers (45, 46) in this field, and the one to be detailed has been found particularly efficacious by the writer.

(*a*) *Muscular Relaxation.*—In the first place, active relaxation of the limb muscles and eventually those of the trunk and face must be practised. It is referred to as active relaxation, because mental activity is required, at first at any rate, to produce the desired result. Easy as it may sound, in point of fact it is quite the most difficult goal to attain in the whole series of exercises.

It is probable that some of the benefit to be derived from muscular relaxation is

referable to the sedative effect which this has on the central nervous system. The constant state of alertness and apprehensiveness which characterizes the asthmatic is lulled to such an extent that when proficiency is attained it is not uncommon for the patient to fall asleep in the course of the exercise.

This soothing effect on the higher centres, including that of the vagus, has been recognized for centuries. Muscular relaxation was practised by Buddhists, in preparation for many hours of contemplation of abstract subjects; by theosophists for the same purpose, and by fakirs in the initiation of their amazing production of almost complete suspension of animation.

Another desirable result is the return of the thoracic muscles from a state of excessive postural tonicity to that of remarkable laxity. It must be obvious that such a change produces an ideal state for the subsequent manipulations of the masseuse.

In preparation for this exercise the patient should lie down on a comfortable couch in a room from which all noise and bright light are excluded. He should then attempt to voluntarily relax certain groups of muscles con-

trolling a distal joint, such as the ankle. The success or failure is demonstrated to him by occasional attempts to move the foot passively. At first it will be found that increased resistance is offered, but as the conception of the desired state gradually dawns on the patient's mind so it will be found that the limb approaches more and more to that of a lifeless member.

After many days of practice relaxation will be extended to all limbs, which should then be capable of being moved about like inanimate objects. The lower jaw droops, the eyelids are half closed, the eyeballs turn upwards, the face becomes expressionless and the abdominal wall as resistanceless as that of the visceroptotic multipara. Respiration is smooth, shallow and inaudible.

Although the mind is at first actively engaged on the production of this state, for which reason it is referred to as an exercise, yet as proficiency increases the patient is able to reproduce extreme relaxation with scarcely a volitional effort, thus allowing, as it were, a relaxation of mental as well as muscular tone.

One other point should be remembered. After the first attempts it will be found most helpful if the patient takes slow deep breaths

during the induction of the relaxed state. When this aim has been achieved, respiration naturally assumes a shallower character.

At first the individual sittings should not last longer than ten minutes, but as advance is made they may be extended to half an hour or more. The sensation of renewed vigour and well-being which follows this practice is not the least noteworthy of its results.

There is, of course, no need for a physician or masseuse to be present on each occasion. Once the patient has fully grasped the essential requirements, he can practise at home at any convenient hour.

Some asthmatics attain such a high degree of muscular control that they can induce a relaxed condition at the first warning of an attack and often inhibit its development.

Finally it should be noted that the achievement of success is intimately dependent on the intelligence of the patient. It requires an immense amount of time and patience to teach the rudiments of relaxation to the hospitals class of patient (meaning the class which used to preponderate at these institutions before it was crowded out by the middle and comparatively affluent members of the com-

munity), and in addition the provision of sufficient workers and quiet rooms at hospitals is seldom possible. However, the attempts should always be made to produce some degree of relaxation before passing on to the next stages of treatment.

(*b*) *Mobilization of Chest Wall and Shoulder Girdles.*—Although all the exercises produce this result to a greater or less degree, certain movements are employed solely for the purpose.

Undue elevation of the shoulders presents the first difficulty, and suppleness must be restored to this region by swinging movements of circumduction at the shoulder joints.

Active depression of the shoulder girdle must now be taught, and as the patient will fail to comprehend the exact movement to be carried out, it is wise to start the exercise by a slight shrug, followed by the opposite movement, which then becomes clear to him. Incidentally downward traction is accompanied by an expiratory jerk, which is all to the good in that it tends to reduce alveolar distension.

Freedom of spinal movement, particularly in the direction of extension, is restored by various exercises of stooping, twisting and extension,

at first singly, but later in combination. These exercises necessarily affect advantageously the entire series of costal articulations.

An effective measure designed to promote spinal flexibility is carried out by the patient supported on knees and hands. The spine is then vigorously flexed and extended, rather with the movement of a bucking horse. This may be followed by the patient's lying down in the prone position, and making rhythmic efforts to approximate the occiput and the feet as in an exaggerated "swallow dive."

Spinal rotation is best performed in the sitting posture, otherwise hip movement is apt to enter too much into the exercise.

The patient's arms are held away from the body with the fingers resting lightly on the table. The head and shoulders are then swung to one side and the other, the arms following the movement and acting by their inertia as a slight drag whose effect is increased at the moment of reversal of direction.

These and several other exercises are carried out at first for a few minutes only, later for longer periods, but in every case massage should be given between individual groups of move-

ments and not at the end of the series. The alternation of exercise and massage is most important in counteracting any tendency which muscular work may have to produce stiffness, at the same time allowing the patient to rest from his recent exertions.

In order to promote rhythmicity and lessen any sense of fatigue the exercises should be carried out to the accompaniment of music. This method, introduced at Guy's Hospital by Miss Angove (46), has proved eminently successful, the only expense involved being for gramophone and records.

(*c*) *Respiratory Gymnastics.*—In asthma and emphysema it is desirable that the power and extent of expiration should be increased. It should be remembered that even when true emphysema is present, yet much of the respiratory embarrassment is referable to the preceding state of over-distension. It is this and not the emphysema which can be benefited by forced expiration.

These facts have been appreciated and worked upon for some years at Mont Dore and have profoundly influenced the treatment of chronic asthmatics in this country since their publication by Hurst (45) three years ago.

Each breathing exercise consists of three and a half respiratory cycles. The patient commences with a forced expiration, followed by gentle inspiration again followed by forcible expiration, and so on, the cycle closing on the expiratory phase. Note that nearly all patients when told to start by breathing out immediately take a deep breath. This tendency must be looked for and abolished.

Air is drawn through the nose and expelled through the mouth. It is usual for the tongue and teeth to be in the position for the sounding of the letter S, thereby producing a hissing sound on expiration. The only point in this is that audibility of expiration assists the patient in the performance of the exercise, and helps the masseuse in the regulation of the amount of assistance which she brings to bear.

The part which she plays is the reinforcement of the patient's efforts by the application of "thoracic shaking." This movement is only acquired by dint of considerable practice. The hands of the masseuse are placed on the antero-lateral aspect of the chest, then in the mid-axillary line, over the apices and finally at different levels of the posterior wall. During

expiration only they impart to the chest a brisk in-and-out shaking movement which is intensified towards the end of the respiratory act, thereby aiding yet further expulsion of air from the lungs, an effect which is clearly audible to patient and gymnast. When the hands are on the back of the thorax, the patient is encouraged to bend over them in an attempt to correct the acquired kyphosis.

All these exercises can be learned by the patient, who should then carry them out at his home. Even the chest-shaking movement can be performed quite well by his own hands. In addition to daily practice, the expiratory exercises should always be given shortly after the termination of a paroxysm.

Where asthma is dependent upon or associated with gross lesions of the lungs other than emphysema, certain additions to and modifications of the course are required. These are dealt with when considering the treatment of complications.

CHAPTER XI

TREATMENT OF COMPLICATIONS

Bronchitis.—Bronchitis sooner or later appears in the majority of asthmatics, thereby occasioning more frequent outbursts of broncho-spasm, dyspnœa and cough, even in the interparoxysmal intervals.

For the bronchitic asthmatic the question of suitable climate is all-important. High altitudes such as are beneficial in pure asthma can rarely be advised in the presence of bronchitis. A clear, dry atmosphere with plenty of sunshine is indicated, and where funds permit the patient should winter abroad, preferably in Helouan or Assuan. Madeira and the Canaries also answer the purpose quite well, but leave much to be desired in the way of sanitation and general cleanliness. The Balearic Islands are usually blest with good weather, although the climate is less favourable than that of the preceding localities. They have the advantage of proximity to Europe and relatively cheap living.

Malaga and Bordighera and the neighbouring villages offer suitable havens for the bronchitic, but the French Riviera should be avoided. Not only do the winters in the south of France appear to be becoming more rigorous in nature, but also this area is a hotbed of catarrhal infections and is usually visited by extensive outbreaks of influenza.

If wintering abroad, the patient must make up his mind to stay away until the end of April. A common mistake is to return in late March, only to meet cold winds and treacherous fluctuations of temperature which immediately cause an outburst of acute bronchitis and asthma.

If unable to go abroad, asthmatics must make the best of the South Coast, excluding that which lies east of Seaford.

Drugs are of some value in rendering sputum less tenacious and reducing cough, consequently less provocative of asthmatic attacks. Thus when cough is a prominent symptom the following may be prescribed :

℞ Liq. picis. aromat. . . . ℥xxv
Syr. codein. . . . . ʒss
Syr. prun. Virgin. . . . ʒss.
Infus. cascarillæ . . . ad. ʒss.

Sig. : ʒ t.d.s. p.c. ex. aq.

A useful expectorant mixture is :

℞	Vin. antimonial	℥xv
	Ammon. chlor.	gr. x
	Diamorph. hydrochlor.	gr.1/30
	Spr. chloroform	℥x
	Spr. aurant.	ʒss.
	Aq. chloroform	ad. ʒss.

Sig. : ʒss. four-hourly ex. aq.

The quantity of heroin may call for reduction, but it is a valuable drug if given in sufficient quantity to allay excessive coughing whilst avoiding undue depression of the respiratory centres.

Of greater efficacy in the treatment of chronic bronchitis are certain forms of inhalation. Good results cannot be expected from the application of a mask soaked in medicament to the patient's face. A reliable nebulizer using oxygen as the basis is demanded. With such apparatus creosote, pine oil, eucalyptus oil and adrenalin can be converted into the finest vapour and inhaled into the lowest reaches of the respiratory tract without embarrassment.

The use of vaccines in bronchitic asthma has already been fully described. It should be regularly included in the yearly treatment.

Acute exacerbations of bronchitis demand careful supervision. As they usually usher

in a severe paroxysm of asthma, adrenalin should be given at once, followed by the exhibition of ephedrine four-hourly. The patient must remain in his bedroom, but not necessarily in bed. The temperature of the room must be kept at 60 to 65° F. day and night. This is most important, any chilling of the air being invariably followed by a relapse on the part of the patient.

A steam kettle must be in constant use, the following mixture of volatile oils being added to the water.

℞	Ol. pini Sylvest.	℥x
	Tr. benzoin co.	ʒss.
	Ol. santali.	℥x
	Ol. terebinth	℥xv
	Creosote	℥xv
	Ol. eucalyt.	℥xv
	Industrial spirit	ad. ℥j

Sig.: A teaspoonful to be added to each pint of water in the kettle.

The painful cough responds to such a preparation as :

℞	Pot. iod.	gr. v
	Pot. bicarb.	gr. xv
	Pot. cit.	gr. xx
	Codein. sulph.	gr. ¼
	Tr. belladon.	℥x
	Syr. aurant	ʒss.
	Aq. menth. pip..	ad. ℥ss.

Sig.: ℥ss. four-hourly ex. aq.

Local applications to the chest are of unquestionable value in relieving the sensation of substernal rawness and constriction. The old-fashioned linseed poultice serves this purpose well, and should be followed by wrapping the part in warmed cotton-wool.

Dover's powder is the ideal remedy for sleeplessness due to cough and pain and should be prescribed if the sputum is as yet scanty. Unfortunately an appreciable number of patients are excessively nauseated by the contained ipecacuanha. If this be the case, $\frac{1}{20}$ grain of heroin should be substituted for the powder.

Remedial exercises as described in the previous chapter should be carried out in all cases of chronic bronchitis, and when the sputum is copious, or when bronchiectasis co-exists, the chest-shaking manœuvre must be performed with the patient lying prone across the bed or couch. The hands support the body by resting on the floor; the trunk inclines downwards, whilst the other point of support is provided by the pelvis and legs in contact with the couch.

Gravitational drainage is thus promoted, and

large quantities of sputum may be expelled in this manner.

In addition to chest shaking, the masseuse carries out the practice of thoracic clapping. A series of short, quick strokes is applied at various points of the chest wall. This appears to be particularly efficacious in loosening tenacious sputum by the explosive expulsion of small volumes of entrapped air.

Where sputum is difficult of removal, the clapping action should precede that of shaking.

In debilitated and elderly asthmatics the position for postural drainage will not be tolerated for more than a few minutes. The condition of the pulse must be carefully watched in such cases.

In patients of this type it is well to give general massage and limb exercises in addition to those specifically adapted to meet the asthmatic requirements.

Nourishing food taken frequently in small quantities together with cod-liver oil should be enjoined for the debilitated subject. Here again glucose is an admirable aid to the desired end.

Emphysema.—It has been noted that true

emphysema in which destruction of lung substance has taken place is incapable of remedy; nevertheless, every effort should be made to reduce the rate of spread of the disease, and to maintain the circulation in as high a state of efficiency as possible.

As emphysema resulting from asthma is almost always combined with bronchitis, much of that which has already been written applies with equal force here.

The respiratory gymnastics not only retard the development of textural atrophy, but also aid in reducing the impediment opposed to the lesser circulation by the attenuated pulmonary capillary bed.

In fact, attention now becomes centred on the cardio-vascular system as a whole.

General massage, with firm muscle kneading and resisted exercises are most helpful in aiding venous return. The importance of congestion of the splanchnic area must not be overlooked, and movements aiming at increasing the tone of the abdominal musculature should form part of the scheme of physiotherapy.

For like reasons the diet must be carefully controlled, both as regards quantity and quality.

In general, fats, meat, spices, alcohol and uncooked vegetables should be forbidden.

The bowels, if confined, are best controlled by saline cathartics aided once or twice weekly by a night dose of half to one grain of calomel.

Climatic considerations are similar to those for bronchitis, but if the latter disease is relatively slight, considerable benefit may be derived from high altitudes, particularly in the warmer months of the year.

Good results have been reported from the use of compressed-air chambers at Reichenhall Spa. The patient is subjected to an air-pressure gradually raised to nearly twice that of the atmosphere. Having maintained this height for half to one hour, it is very gently allowed to return to normal. The action is enhanced by the addition of an extra 20 per cent. of oxygen.

Apart from the increased oxygen proportion, it is difficult to explain the advantage of this system of treatment, unless it be that a high atmospheric pressure diminishes congestion and tendency to spasm of the bronchi.

Even before congestive heart failure manifests itself, the engorged venous system responds well to venesection, a measure which

is doubly indicated when signs of cardiac defeat are evident.

Periodic venepuncture often gives greater relief to the emphysematous asthmatic than all the other forms of treatment put together. According to the general condition of the patient, half to one pint of blood is extracted through a wide-bore needle, the process being repeated three or four times yearly.

The rapid improvement in colour, breathing, digestion and urinary output following this measure is truly remarkable.

Cardiac Failure.—In cases of heart failure, the patient must, of course, be put to bed, and after venesection it is certainly advantageous to administer digitalis, squills and mercury. A useful combination is :

℞ Pulv. scillæ . . . . grs. ij
Digitalis foliæ . . . . grs. iss.
Hydrag. subchlorid . . . gr. ½

Ft. cachet. One to be taken thrice daily.

Nasal administration of oxygen should also be carried out by means of a fine rubber catheter passed into the naso-pharynx.

Sleep can usually be procured by means of paraldehyde, provided that it be given in suffi-

ciently large doses, e.g. 4 drachms. It is well tolerated by patients with heart failure, who seem to be less aware of its odour than those in attendance on them.

If active bronchitis be present accompanied by temperatures above 100° F., paraldehyde should be given with caution, because pyrexial patients are peculiarly liable to become restless and unmanageable after taking this drug.

Chloral and bromide in 20-grain doses or medinal may then be tried, but chloral should not be given daily for long periods. Only in exceptional cases is it wise to prescribe derivatives of the opium group.

When the patient is convalescent, it is essential that prior to his leaving his bed he should be given graduated "cardiac exercises" by a competent masseuse.

Briefly these consist of muscle kneading, followed by free movements of the limbs, again followed by resisted exercises. The rate of progression and the degree of resistance imposed by the attendant are regulated by the effect on the pulse rate. If the latter shows a progressive rise, the exercises must be curtailed. If, on the other hand, the pulse rate

falls towards normal, the movements may be more vigorous.

To allow any " cardiac " patient to leave his bed for couch or chair without this preliminary training represents the height of folly, and results, as often as not, in a relapse.

CHAPTER XII

RESULTS OF TREATMENT

SOME of the results to be expected from certain forms of treatment of asthma have already been discussed when considering prognosis. It may not be out of place, however, to summarize as far as possible the records of experience of the many workers in this field of medicine.

Generally it may be accepted that careful regulation of the quantity and quality of the food and the times of food intake will amply repay the trouble taken in all types of asthmatics.

Elimination of focal sepsis and suspected sources of reflex vagal stimulation seldom produces striking results. Rackemann and Tobey (19), reviewing the results of treatment in this connection, conclude that :

(1) 28 per cent. of patients gave a history of a previous operation on the nose or throat without regard to the cause of asthma as found.

(2) True foci of infection in the nose, throat and teeth were discovered in 44 per cent. of all cases.

(3) The presence of septic foci bears but little relationship to the outcome of asthma.

(4) The gross results of eradicating these foci are disappointing in comparison with those produced in patients in whom the foci are left alone.

(5) Local treatment of nose, throat and teeth gives permanent relief from asthma in 5 per cent. of cases.

(6) Local lesions of the nose and throat may develop from the same fundamental cause as that of asthma: e.g. repeated rhinorrhœa may give rise to the formation of polypi.

Lyon and Murray-Lyon (18) are equally of the opinion that the results of operation on the nose or throat are disappointing, and advise that such treatment should only be recommended to relieve definite local symptoms.

Vaccine therapy in suitable cases is often highly efficacious, particularly if combined with inhalation treatment and wintering in a favourable environment.

Specific and non-specific desensitization is, as a rule, disappointing in the results

obtained. The former is the most hopeful, provided that hypersensitiveness to only one substance can be demonstrated.

Similarly for this type the avoidance of the allergen, if it be compatible with the occupation of the individual, may result in complete cessation of asthmatic attacks. In any case, it should be remembered that asthmatics of this class are definitely in a minority.

Permanent residence at high altitudes can be relied upon to abolish the paroxysms in nearly every case. It is not to be recommended, however, in the presence of bronchitis of any severity. Furthermore, the number of patients who can avail themselves of such an opportunity is necessarily restricted.

For actino-therapy, diathermy, X-rays and psycho-analysis the scope is very limited. They can all be useful, but chiefly in the sense of reinforcement of more radical treatment.

The majority of drugs are of use merely to hold symptoms in check, and have no value in eliminating or correcting the asthmatic tendency.

Exceptions to this statement are possibly presented by calcium and irradiated ergosterol, glucose and ammonia. As has been explained,

their use is based upon the results of biochemical investigations of the asthmatic, and may well assist in the correction of fundamental abnormalities. These substances, as also attempts at desensitization by means of urinary proteose, deserve the greatest attention and full trial. The verdict as to their usefulness must be postponed until more extensive experience justifies the enunciation of conclusions on the subject.

Physical exercises and respiratory gymnastics cannot cure the asthmatic, but can and do materially retard the development of organic changes and lengthen the interparoxysmal intervals. They should therefore be employed in all but the mildest cases.

As to the results of treatment of complications, too much cannot be expected, for their very presence indicates structural damage which is irrevocable.

Change of climate and vaccine and inhalation therapy often hold bronchitis at bay.

Remedial exercises lessen the distress due to emphysema. Yet all treatment becomes progressively less curative and more palliative with lengthening history of disease and appearance of textural decay, until signs of cardiac

defeat herald the final triumph of asthma over its victim.

In no other disease is greater concentration on detail demanded of the physician. In no other illness are we so often disappointed when victory seems to be ours. Yet when we look back on the fruit of the labours of the past twenty years we cannot but be impressed by the material advance which has been made towards the ultimate conquest of this mysterious malady.

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